THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE HEMISPHERX BIOPHARMA, INC. LITIGATION	:	CIVIL ACTION NO.: 09-05262

ORDER

AND NOW, this _____ day of _____, 2010, upon consideration of defendants' Motion to Dismiss the Consolidated [Amended] Class Action Complaint for failure to state a claim upon which relief can be granted, and any opposition and replies thereto, it is hereby **ORDERED** that defendants' Motion is **GRANTED**. It is further **ORDERED** that the Consolidated [Amended] Class Action Complaint is **DISMISSED WITH PREJUDICE**.

BY THE COURT:

_____
Diamond, J.

THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE HEMISPHERX BIOPHARMA, INC. LITIGATION	:	CIVIL ACTION NO.: 09-5262

DEFENDANTS' MOTION TO DISMISS
CONSOLIDATED [AMENDED] CLASS ACTION COMPLAINT

Defendants Hemispherx Biopharma, Inc., William A. Carter, M.D. and David R. Strayer, M.D., by their attorneys, respectfully move this Court to dismiss with prejudice plaintiffs' Consolidated [Amended] Class Action Complaint ("Amended Complaint") pursuant to the Private Securities Litigation Reform Act of 1995 ("PSLRA"), 15 U.S.C. § 78u-4(b), and Federal Rule of Civil Procedure 12(b)(6), and for the reasons set forth below and in the accompanying memorandum of law:

1. The Amended Complaint must be dismissed because it fails to plead a misstatement or omission with the specificity mandated by the PSLRA;

2. The Amended Complaint must be dismissed to the extent it is based on non-actionable statements of belief, forward-looking statements protected by the PSLRA's safe harbor, or statements of optimism;

3. The Amended Complaint must be dismissed because it fails to state with particularity facts giving rise to a strong inference that defendants acted with scienter, as required under the PSLRA; and

4. Plaintiff's claims against the individual defendants must be dismissed because its allegations of "control person" liability are wholly derivative of its claims of securities fraud, which are deficient as a matter of law.

Respectfully submitted,

/s/ Robert L. Hickok

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March 12, 2010

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE HEMISPHERX BIOPHARMA, INC. LITIGATION	:	**CIVIL ACTION NO. 09-CV-5262**

MEMORANDUM OF LAW IN SUPPORT OF DEFENDANTS' MOTION TO DISMISS PLAINTIFF'S CONSOLIDATED [AMENDED] CLASS ACTION COMPLAINT

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In its Consolidated [Amended] Class Action Complaint ("Amended Complaint"),[1] Lead Plaintiff the Hemispherx Investor Group[2] ("plaintiff") seeks damages for alleged violations of Section 10(b) of the Securities Exchange Act of 1934 ("Section 10(b)"), Rule 10b-5 promulgated thereunder by the Securities and Exchange Commission ("SEC"), and Section 20(a) of the Exchange Act ("Section 20(a)").[3] Plaintiff purports to represent a class of all purchasers of Hemispherx common stock between February 18, 2009 and December 1, 2009 (the putative "Class Period"). (Exh. 1, Am. Compl. ¶ 1.)

Pursuant to the Private Securities Litigation Reform Act of 1995 ("PSLRA" or "Reform Act"), 15 U.S.C. § 78u-4(b), and Federal Rule of Civil Procedure 12(b)(6), defendants Hemispherx Biopharma, Inc. ("Hemispherx" or "the Company"), William A. Carter, M.D., and David R. Strayer, M.D. (collectively "the individual defendants" and, with Hemispherx, "defendants"), by their attorneys, hereby submit this memorandum of law in support of their motion to dismiss the Amended Complaint for failure to meet the rigorous pleading requirements of the PSLRA.

I. INTRODUCTION[4]

Hemispherx is a small biopharmaceutical company headquartered in Philadelphia, Pennsylvania. Founded in the early 1970s, Hemispherx develops new drug therapies based on

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[1] A copy of the Amended Complaint is included in the Appendix being filed herewith as Exhibit "1." Hereinafter, each document cited herein and contained in the Appendix is accompanied by an "Exh." reference.

[2] The Hemispherx Investor Group consists of the following Hemispherx shareholders: Victor Cherry, Ehud Nahum, Jagvinder Pal Singh and Padmakar Boienipelly. (Exh. 1, Am. Compl. ¶ 1.)

[3] *See* Exh. 1, Am. Compl., Counts I and II.

[4] The Factual Background, Section II below, describes the events outlined in this Introduction in more detail, providing citations to the Amended Complaint and documents the Court may consider on a motion to dismiss. *See infra* Sections II & III.C.

natural immune system enhancing technologies for the treatment of viral and immune based chronic disorders. One of the Company's core products is Ampligen®, an experimental drug being developed for the treatment of Chronic Fatigue Syndrome ("CFS"), a "debilitating chronic illness characterized by profound all-encompassing physical and mental fatigue that is not improved by rest."[5]

Hemispherx originally filed its New Drug Application ("NDA") for Ampligen® with the United States Food and Drug Administration (the "FDA" or "Agency") on October 11, 2007. On December 5, 2007, the FDA issued a "refusal to file" letter, notifying the Company that its NDA was insufficiently complete to permit a substantive review. Hemispherx promptly disclosed the FDA's decision in a press release and, a few days later, hosted an investor conference call during which Dr. Carter provided a detailed explanation of the deficiencies the FDA had found in the Ampligen® NDA.

Over the course of the next four months, Hemispherx submitted responses to the FDA's filing questions as well as five additional amendments to its NDA. On July 8, 2008, the FDA accepted the Ampligen® NDA for substantive review. Under the Prescription Drug User Fee Act ("PDUFA"), the Agency's deadline for completing the review was February 25, 2009.

On July 17, 2008, Hemispherx hosted an conference call for the purpose of explaining to investors the FDA substantive review process. Dr. Carter advised that the Company would be answering questions raised by the Agency and that it may take up to six months, or until mid-January 2009, for Hemispherx to provide the necessary data to the FDA.

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[5] Exh. 104, CDC, Chronic Fatigue Syndrome Booklet at 1, *available at* http://www.cdc.gov/cfs/pdf/06_103087_dtp_cfs_booklet-spread.pdf (last visited Mar. 11, 2010) (recognizing that, in addition to fatigue, persons with CFS may experience "unrefreshing sleep, impaired memory and concentration, muscle and joint pain, sore throat, headache, tender lymph nodes, and an increase in symptoms and malaise extending 24 hours after physical or mental activity") (hereinafter "CFS Booklet").

As late as January 29, 2009, Dr. Carter publicly stated in an interview that additional tests were being conducted and that it likely would take 4-8 weeks to complete those tests.

In a February 18, 2009 press release, Hemispherx announced that the FDA had extended the PDUFA date by three months until May 25, 2009 because the Company had submitted new data to the Agency, which needed more time to review the submission. On May 26, the Company announced that it had been advised by the FDA that, due to staff scheduling changes, the Agency may need an additional two weeks to complete its review of the NDA. Yet, two weeks came and went, as did the summer and fall, and Hemispherx still had not received a decision from the FDA.

In September 2009, a financial blogger named Adam Feuerstein challenged Dr. Carter during an analyst conference for not aggressively hounding the FDA about its delayed decision on the Company's NDA. In response, Dr. Carter explained that the Company was having regular interactions with FDA reviewers, and that it was Hemispherx's belief that "in the good space of time, the FDA will respond to us much like they do with all other companies."[6]

In addition to providing ongoing reports of the status of the NDA process to its investors, Hemispherx issued a press release on November 2, 2009, summarizing the information the Company had been providing all along regarding its preclinical animal testing and its efforts to respond to prior FDA inspections of its Spokane facility. The next day, Mr. Feuerstein published an article on his blog, entitled "Hemispherx Cops to Ampligen FDA Delay,"[7] in which he falsely accuses Hemispherx and Dr. Carter of lying to investors about the status of the

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[6] Exh. 75, 09/11/09 Conf. Call Tr. at 5.

[7] *See* Am. Compl. ¶ 75; Exh. 102, 11/03/09 TheStreet.com article; "Hemispherx Cops to Ampligen FDA Delay," *available at* http://www.thestreet.com/story/10620979/1/hemispherx-cops-to-ampligen-fda-delay.html (last visited Mar. 11, 2010).

Ampligen® NDA and falsely suggests that the Company's NDA had not in fact been accepted for review by the FDA.

Predictably, within a week after Mr. Feuerstein published his demonstrably false article, the first of five securities fraud lawsuits was filed in this Court against Hemispherx and Dr. Carter. Each of these lawsuits alleged claims arising solely from Mr. Feuerstein's hostile and speculative rantings – ***not*** from any actual conduct by Hemispherx or Dr. Carter. These claims, now embodied in Lead Plaintiff's Amended Complaint, are based on – and quote from – Mr. Feuerstein's rantings instead of any actual misrepresentation by defendants. Because the Amended Complaint is based on the false and misleading blog reports by Mr. Feuerstein, the Amended Complaint itself is fundamentally defective and fails to state any claim under the federal securities laws.

Because plaintiff claims that defendants violated the federal securities laws by allegedly misrepresenting or failing to disclose material information regarding the status of the Company's Ampligen® NDA, this memorandum provides an overview of the new drug regulatory context in which Ampligen® was developed and submitted for approval.[8] The memorandum then presents the following grounds on which plaintiff's claims must be dismissed:

First, the Amended Complaint fails to plead a misstatement or omission of material fact with the particularity required under the PSLRA. Not only does the Amended Complaint allege no contemporaneous facts showing that the statements in question were false or misleading when made, but most of the allegedly omitted information was promptly and fully

[8] *See infra* Section II.

disclosed by defendants before or during the putative Class Period, or was not material in light of prior disclosures.[9]

Second, most of the allegedly fraudulent statements are non-actionable statements of belief or opinion, forward-looking statements protected by the PSLRA's safe harbor provisions, or statements of optimism.[10]

Third, the Amended Complaint fails to meet the PSLRA's heightened requirements for pleading a strong inference of scienter.[11]

For each of these separate and independent reasons, plaintiff's Section 10(b) claim, set forth in Count I of the Amended Complaint, must be dismissed in its entirety. And because plaintiff's Section 20(a) claim is purely derivative of its Section 10(b) claim,[12] Count II must be dismissed as well.

II. FACTUAL BACKGROUND[13]

A. Overview Of Prescription Drug Approval Process

Before a biotechnology company, pharmaceutical company or other drug sponsor (hereinafter "sponsor" or "applicant") can legally market or sell a new prescription drug in the United States, the sponsor must obtain approval from the Food and Drug Administration (the "FDA" or "Agency") pursuant to the requirements of the Federal Food, Drug, and Cosmetic Act

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[9] *See infra* Section IV.A.

[10] *See infra* Section IV.B.

[11] *See infra* Section IV.C.

[12] *See infra* Section IV.D.

[13] This Factual Background is drawn from the Amended Complaint's factual allegations, which are accepted as true solely for purposes of this motion, and from documents contained in the accompanying Appendix, which materials, as explained *infra* in Section III.C, the court may consider when deciding defendants' motion to dismiss.

("the Act") and FDA regulations promulgated thereunder. *See, e.g.*, 21 U.S.C. § 355 (2005); 21 C.F.R. § 314 (2005).[14] To obtain FDA approval of a new drug, the sponsor must successfully pass several critical milestones, including preclinical (laboratory and animal) testing, three phases of clinical (human) trials (studies), and the submission of a New Drug Application ("NDA"). *See generally* 21 C.F.R. § 314.[15] The "FDA estimates that it takes approximately eight-and-a-half years to study and test a new drug before it can be approved for the general public." (Exh. 88, CDER Handbook at 5.)

1. The Purpose Of An NDA

The development of a new drug begins with preclinical trials and an investigational new drug ("IND") application followed by Phase 1, 2, and 3 clinical trials. During the preclinical phase, "the sponsor's primary goal is to determine if the product is reasonably safe for initial use in humans, and if the compound exhibits pharmacological activity that justifies a commercial development."[16] During clinical trials, "an investigational compound is administered to humans and is evaluated for its safety and effectiveness in treating, preventing, or diagnosing a specific disease or condition." (Exh. 88, CDER Handbook at 7.)[17] Once a

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[14] *See also* Exh. 88, U.S. Dep't of Health & Human Serv., FDA, Center for Drug Evaluation and Research ("CDER"), The CDER Handbook, at 19-28 (Revised: 03/16/98) (formerly *available at* http://www.fda.gov/cder/handbook) (hereinafter "CDER Handbook"). Although the CDER Handbook has been removed from the FDA website while the Agency revises it, *see* http://druganddevicelaw.blogspot.com/2009/08/fdas-cder-handbook-undergoing-revision.html, it was in effect during the time period when Hemispherx was conducting its preclinical and clinical trials and while it was preparing its NDA and continues to represent an accurate description of the new drug development and review process under the Act.

[15] *See also* Exh. 88, CDER Handbook at 4-28.

[16] Exh. 77, FDA Investigational New Drug (IND) Application, *available at* http://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/default.htm (last visited Mar. 11, 2010) (hereinafter "IND Application").

[17] .*See also* 21 C.F.R. § 314.126(a) ("The purpose of conducting clinical investigations is to distinguish the effect of a drug from other influences, such as spontaneous change in the course of the disease, placebo effect, or biased observation.").

sponsor has completed the Phase 3 clinical studies and performed the necessary analysis and meta-analysis of the data collected from the study, it will submit an NDA to the FDA. *See* 21 C.F.R. § 314.1-314.560 (providing regulations for NDAs); 21 C.F.R. §§ 314.50 (delineating required content and format for NDAs).[18]

The FDA will approve an NDA "after it determines that the drug meets the statutory standards for safety and effectiveness, manufacturing and controls, and labeling." 21 C.F.R. § 314.105(c). When assessing whether an NDA should be approved for marketing in the United States, the FDA will decide:

- Whether the drug is safe and effective for its proposed use(s), and whether the benefits of the drug outweigh its risks.
- Whether the drug's proposed labeling is appropriate, and, if not, what the drug's labeling should contain.
- Whether the methods used in manufacturing the drug and the controls used to maintain the drug's quality are adequate to preserve the drug's identity, strength, quality, and purity.

(Exh. 88, CDER Handbook at 7.)

2. The FDA's Acceptance Or Refusal Of An NDA For Filing

Within 60 days of receiving an NDA, the FDA will determine whether the application "may be filed." 21 C.F.R. § 314.101(a)(1). If the FDA accepts the NDA for filing, it means that the Agency "has made a threshold determination that the application is sufficiently complete to permit a substantive review." 21 C.F.R. § 314.101(a)(1).

[18] *See* FDA New Drug Application, *available at* http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/NewDrugApplicationNDA/default.htm (last visited Mar. 11, 2010).

The FDA may refuse to file an NDA, however, if "[t]he application . . . is incomplete because it does not on its face contain information required under section 505(b), section 505(j), or section 507 of the act and 314.50 or 314.94." 21 C.F.R. § 314.101(d)(3). The FDA has exercised its authority under this provision in three circumstances:

> (1) omission of section of the NDA required under 21 CFR 314.50 or presentation of a section is so haphazard a manner as to render it incomplete on its face. . . .
>
> . . . .
>
> (2) clear failure to include evidence of effectiveness compatible with the statute and regulations, for example:
>
> > (a) ***lack of an adequate and well-controlled studies [21 CFR 314.126] [sic], including use of obviously inappropriate or clinically irrelevant study endpoints. . .***
> >
> > (c) ***use of a study design clearly inappropriate (as reflected in regulations or well-established agency interpretation) for the particular claim . . .***
>
> (3) omission of critical data, information or analyses needed to evaluate effectiveness and safety or provide adequate directions for use, for example:
>
> > a) ***omission, without explanation, of animal carcinogenicity studies for a chronically administered drug. . . .***
> >
> > . . . .
> >
> > c) total patient exposure (numbers or duration) at relevant doses that is clearly inadequate to evaluate safety,
> >
> > d) ***clearly inadequate evaluation for safety and/or effectiveness of the population intended to use the drug, including pertinent subsets, such as gender, age, and racial subsets,***

> e) absence of a comprehensive analysis of safety data, e.g., as recommended in the Clinical/Statistical Guideline.[19]

3. Waivers Allowed Under Certain Circumstances

While an NDA generally must be supported by adequate and well-controlled studies, an applicant may request that the FDA waive any criteria of an adequate and well-controlled study "either prior to the investigation or in the evaluation of a completed study." 21 C.F.R. § 314.126(c). *See also* 21 C.F.R. § 314.90 (permitting waiver of well-controlled study). The FDA may grant a waiver under three circumstances:

> (1) The applicant's compliance with the requirement is unnecessary for the agency to evaluate the application or compliance cannot be achieved;
>
> (2) The applicant's alternative submission satisfies the requirement; or
>
> (3) The applicant's submission otherwise justifies a waiver.

21 C.F.R. § 314.90(b)(1)-(3).

4. Prescription Drug User Fee Act (PDUFA) Timelines

If the FDA accepts an NDA for filing, it will seek to review the application within 180 days of receipt and "send the applicant either an approval letter under § 314.105 or a complete response letter under § 314.110." 21 C.F.R § 314.100(a). This 180-day period is called the "initial review cycle." *Id.*

Pursuant to the Prescription Drug User Fee Amendment of 2007 (PDUFA IV), the FDA agreed to meet specific performance goals,[20] including to "[r]eview and act on 90 percent

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[19] Exh. 81, New Drug Evaluation Guidance Document: Refuse to File at 4-5 (dated July 12, 1993), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM080561.pdf (last visited Mar. 11, 2010) (emphasis added).

[20] *See* Manual of Policies and Procedures, CDER, Office of New Drugs: NDA and BLAS: Communication to Applicants of Planned Review Timelines, *available at*,

(continued...)

of standard original NDA . . . submissions within 10 months of receipt."[21] However, in December 2008, the FDA reported that it had been "struggling to meet PDUFA goals for the past several years." (Exh. 83, J. Jenkins, New Drug Review 2008 Update at 13, (Dec. 4, 2008), *available at*, http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ucm117686.pdf (last visited Mar. 11, 2010) (hereinafter "Jenkins Update").) In fact, in 2008, the Agency "made a management decision that [it] would ***not*** be able to meet all PDUFA goals and meet all [its] other priorities." (*Id.* (emphasis added).) Between January 1 and October 31, 2008, the FDA missed its PDUFA goals 20% of the time. (*Id.* at 17.) The stated reasons for missed PDUFA goal dates included "workload/competing priorities" among other issues. (*Id.* at 16.)

5. Information Requests And Discipline Review Letters

During the NDA review cycle, the FDA will request additional information from the drug sponsor through discipline review letters ("DR letters") and information request letters ("IR letters"). (Exh. 105, CDER, Guidance for Industry, Information Request and Discipline Review Letters Under the Prescription Drug User Fee Act, at 1, (November, 2001) *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM172134.pdf (last visited Mar. 11, 2010) (hereinafter "IR/DR Guidance"). The FDA does not consider DR and IR letters to be "action letters," discussed *infra*, "because they do not represent a complete review of the submission and, therefore, do not stop the user fee review clock." (*Id.* at 6.)

(continued...)

http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/ucm081995.pdf (last visited Mar. 11, 2010).

[21] Section A: PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 Through 2012, *available at* http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm119243.htm (last visited Mar. 11, 2010).

The purpose of the DR letter is to provide "early Agency thoughts on possible deficiencies to applicants in a letter as each discipline finishes its initial review of its portion of the pending application . . . ." (*Id.* at 3.) Comments in the DR letter usually reflect input from the review team only, however, and not that of the review division director or office director. (*Id.* at 3, 4.) Indeed, supervisors may add or delete items later when they review the NDA, which may result in more or fewer deficiencies in the action letter. (*Id.* at 4.) Furthermore, once reviews from different disciplines are integrated, "additional concerns might arise or previously stated concerns may be resolved." (*Id.*) As a result, applicants may gather and provide the Agency with information in response to a DR letter that may not ultimately be necessary for the approval of the application. (*Id.*)

The purpose of an IR letter is "to request further information or clarification that is needed or would be helpful to allow completion of the discipline review." (*Id.* at 3) Therefore, unlike DR letters, IR letters are issued while the discipline review is in process. (*Id.*) Like DR letters, they do "not necessarily reflect input from upper supervisory levels." (*Id.*)

Importantly, DR letters and IR letters should not be read as signaling to the applicant whether or not the NDA will ultimately be approved by the FDA. In fact, the Agency's NDA review staff are specifically trained ***not*** to speculate as to what the official regulatory action will be:

> ***A decision on the official regulatory action for an application can be made only after the signatory authority has completed review of the available information*** (e.g., from the action package and consultation with appropriate members of the review team and FDA management). Therefore, it is important that communication with the applicant during the review of an application be generally limited to request for additional information (e.g., information request letters), conveyance of identified deficiencies that need to be corrected before the application can be approved (e.g., discipline review letters), and preliminary comments on draft

> labeling. ***FDA staff should make clear to the applicant that such communications are preliminary and that the official regulatory action for the application has not yet been taken. We discourage applicants from requesting that Agency staff speculate about the eventual official regulatory action. Such requests are premature and can lead to unnecessary tension in the communications between the applicant and the members of the review team.***

(Exh. 80, Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products at 8 (April 2005), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079748.pdf (last visited Mar. 11, 2010) (hereinafter "Review Staff Guidance") (emphasis added).)

6. FDA Preapproval Inspections

The FDA can give final approval to a drug candidate "only if the methods used in, and the facilities and controls used for, the manufacture, processing, packing, and testing of the drug are found adequate to ensure and preserve its identity, strength, quality, and purity." (Exh. 106, FDA, Compliance Program Guidance Manual, Program 7346.832: Pre-Approval Inspections/Investigations, pt. I, at 1 (Aug. 15, 1994), *available at* http://www.fda.gov/downloads/ICECI/ComplianceManuals/CompliancePrograManual/ucm125397.pdf (last visited Mar. 11, 2010.) Where the drug under review is a new chemical or molecular entity or would represent the sponsor's first approved drug, the FDA will generally conduct a product-specific preapproval inspection of the sponsor's manufacturing facilities and clinical trial sites. (Exh. 88, The CDER Handbook at 27-28.)

When conducting a preapproval inspection, FDA will "audit manufacturing-related statements and commitments made in the NDA against the sponsor's manufacturing practices." (*Id.* at 27.) During these inspections, FDA investigators will:

- verify the accuracy and completeness of the manufacturing-related information submitted in the NDA;
- evaluate the manufacturing controls for the preapproval batches upon which information provided in the NDA is based;
- evaluate the manufacturer's compliance with Current Good Manufacturing Practices (CGMPs) and manufacturing-related commitments made in the NDA; and
- collect a variety of drug samples for analysis by FDA field and CDER laboratories. These samples may be subjected to several analyses, including methods validation, methods verification, and forensic screening for substitution.

(*Id.* at 27-28.)

When conducting inspections of a manufacturing facility, FDA investigators are required to record their "inspectional observations" on a Form FDA-483. (*See* FDA, Investigations Operations Manual § 5.2.3 (2006), http://www.fda.gov/ICECI/Inspections/IOM/default.htm (last visited Mar. 11, 2010).) The investigator's inspectional observations, however, do not represent the FDA's determination regarding the facility's compliance with FDA regulations. (*Id.* §§ 5.2.3.1.4, 5.2.3.3.)[22]

7. FDA Action Letters

After the FDA completes its review of a drug candidate, it will either approve the drug or send the applicant a "complete response letter." 21 C.F.R. § 314.101(f); 21 C.F.R.

[22] The FDA's current Good Manufacturing Practices ("CGMP") regulations require that a drug sponsor also "validate" the manufacturing process to be used to produce the drug product under review. "A validated manufacturing process has a high level of scientific assurance that it will reliably produce acceptable product." Generally, however, process validation studies are conducted on multiple, full-size commercial product batches of the product and are therefore deferred until after the NDA for the product has been approved and preparations for commercial product launch have begun. (FDA, Office of Regulatory Affairs, Guidance Document, Sec. 490.100 Process Validation Requirements for Drug Products and Active Pharmaceutical Ingredients Subject to Pre-Market Approval (CPG 7132c.08) (last revised 03/12/04), http://www.fda.gov/ora/compliance_ref/cpg/cpgdrg/cpg490-100.html (last visited Mar. 11, 2010).)

§ 314.100(a).[23] The Agency will approve an application if "it determines that the drug meets the statutory standards for safety and effectiveness, manufacturing and controls, and labeling . . . ." 21 C.F.R. § 314.105(c).

A complete response letter is a "written communication to an applicant from FDA usually describing all of the deficiencies that the agency has identified in an application . . . that must be satisfactorily addressed before it can be approved." 21 C.F.R. § 314.3(b). The FDA will send a complete response letter if it determines that it will not approve the application in its present form for one or more of the reasons listed in 21 C.F.R. § 314.125. 21 C.F.R. § 314.110(a). When possible, the FDA will also recommend actions that the applicant might take to make the application approvable. 21 C.F.R. § 314.110(a)(4).[24]

8. Post-Marketing Studies

Drug sponsors will "frequently perform studies after the FDA approves a product for marketing. The studies are used to gather additional information about product safety, efficacy, or optimal use." (Exh. 87, Guidance for Industry: Reports on the Status of Postmarketing Study Commitments – Implementation of Section 130 of the Food and Drug Modernization Act of 1997 at 3 (Feb. 2006), *available at*, http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm080569.pdf (last visited Mar. 11, 2010) (hereinafter "Postmarketing Guidance").) In certain

[23] Effective August 11, 2008, the Complete Response letter replaced the "approvable," and "not approvable" letters that the FDA previously issued when a drug application was not approved in its present form. (*See* Exh. 85, FDA News Release, "FDA Revises Process for Responding to Drug Applications," (July 9, 2008), *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ucm116920.htm (last visited Mar. 11, 2010); Exh. 86, FDA, Questions and Answers Regarding the Complete Response Letter Rule, *available at* http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084143.htm (last visited Mar. 20, 2010).

[24] *See also* Exh. 84, FDA Guidance, Complete Response Letter Final Rule, *available at* http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084138.htm. (last visited Mar. 11, 2010) (hereinafter "CRL Guidance").

circumstances, the FDA may require postmarketing studies and clinical trials. *See* 21 U.C.S 355(o)(3). Other times an applicant and the FDA may agree, either at the time of approval or after marketing approval has been granted, that the applicant will conduct a postmarketing study "to provide additional information about product risks, benefits, and/or optimal use." (Exh. 87, Postmarketing Guidance at 4.)

B. Relevant Regulatory History Of The Ampligen® NDA

1. Clinical Development Of Ampligen® For The Treatment Of Chronic Fatigue Syndrome

Hemispherx is seeking FDA approval of Ampligen® for the treatment of Chronic Fatigue Syndrome (CFS), a "debilitating chronic illness characterized by profound all-encompassing physical and mental fatigue that is not improved by rest." (Exh. 104, CFS Booklet at 1.) Because there is no known cause of CFS, therapies generally have focused on treating the symptoms rather than the disease itself. (*Id* at 14.) With the constantly evolving scientific research on the causes and treatments of CFS (*see id.* at 8-10), Hemispherx has spent nearly twenty years researching and understanding CFS, culminating in its filing of the Ampligen® NDA. Ampligen® is the first drug in the class of RNA (nucleic acid) molecules under FDA review to treat CFS specifically and not just the symptoms of the illness. (*See* Exh. 8, 2008 Form 10-K at 3.)

The Ampligen® NDA is supported by, *inter alia*, a Phase 2 clinical trial (AMP 502), an ongoing open label study (AMP 511), and a Phase 3 clinical trial (AMP 516). AMP 502 was conducted as a randomized, multi-center, placebo controlled, double-blind study of 92 patients meeting the CDC's case definition of CFS, to measure the response of several laboratory and clinical variables to Ampligen®. (*See* Exh. 108, David R. Strayer, et. al, A Controlled Clinical Trial with a Specifically Configured RNA Drug Poly (I) Poly (C12U), in Chronic

Fatigue Syndrome, Clin. Infect Dis. 1994 Jan;18 Suppl 1:S88-95, *available at* http://www.hemispherx.net/content/rnd/abstract_scientfic.htm (last visited Mar. 11, 2010).) Based upon AMP 502's results, the Agency Health Research Quality ("AHRQ"), a division of Health & Human Services, reported that "Ampligen, an investigational drug that is not approved by the Food and Drug Administration, given intravenously to severely debilitated patients yielded the most promising results" of the new experimental therapies under review. (Exh. 107, AHRQ Report, 42: Defining and Managing Chronic Fatigue Syndrome: Evidence Report/Technology Assessment Number 42, at http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=hserta&part=A58979; 12/12/06 Press Release (announcing AHRQ report findings).[25]

After AMP 502's "promising" results, Hemispherx had an end-of-Phase 2 meeting with the FDA and also met with a specially convened panel of the FDA's Antiviral Advisory Committee to review the Phase 3 clinical trial design. (Exh. 13, 05/03/04 Press Release; *see also* Exh. 14, 10/18/04 Press Release ("The Company [] worked with the FDA on the design of the Phase II clinical trial . . ."). The FDA authorized Hemispherx to begin its Phase 3 trial, AMP 516, in 1998. (*See* Exh. 2, 2006 Form 10-K at 8.)

AMP 516 was a multi-center, double-blind, randomized, placebo-controlled Phase 3 pivotal study of the efficacy and safety of Ampligen®, given twice weekly versus placebo in patients with severely debilitating CFS. (Exh. 13, 05/03/04 Press Release.) The clinical trial randomized 234 patients at 12 centers across the United States to assess the effects of 40 weeks of treatment with Ampligen® in patients suffering from CFS. (*Id.*) The prospectively defined

[25] Ampligen® has also received the following FDA designations: Orphan Drug Product Designation (FDA) and Emergency (compassionate) Cost Recovery Sales Authorization (FDA). (Exh. 8, 2008 Form 10-K at 3.)

primary endpoint was improved physical performance as measured by Treadmill Exercise Tolerance Testing (ETT): Duration. Efficacy can be established by showing a medically significant increase (≥6.5%) in mean exercise duration (baseline compared to week 40) that is statistically significant (p≤0.05) using a statistical method termed "analysis of covariance." (*Id.*)[26]

On May 3, 2004, the Company announced the results of the AMP 516 trial:

> Patients receiving Ampligen for 40 weeks improved exercise treadmill performance 19.4% vs. 5.1% in the placebo group (p=0.022, analysis of covariance with baseline as covariate). ***An "intent to treat" analysis included patients who completed less than 40 weeks. Similar results were obtained with 17.7% improvement in exercise treadmill duration in the Ampligen cohort compared to 4.3% in patients receiving the placebo (p=0.047).*** Improvements in exercise treadmill duration in the patients receiving Ampligen compared to placebo were greater than twice the minimum considered medically significant (6.5%). Moreover, there was no significant difference in the number of serious adverse events, missed dosages or dropouts (i.e., leaving the study prematurely) among patients receiving Ampligen vs. those receiving placebo, suggesting that the experimental drug was generally well tolerated.

(*Id.* (emphasis added).)

On May 3, 2006, Hemispherx reported that the results of the AMP 516 trial had been audited, and that the audited results would be presented at the 5th International Conference on HHV-6&7 in Barcelona, Spain. (Exh. 15, 05/03/06 Press Release.) The Company also referenced the audited results in a December 12, 2006 press release, which stated that "the patients receiving Ampligen® for 40 weeks improved exercise treadmill performance 14.8% in

[26] As alleged in the Amended Complaint, "[a] statistical significance level of 0.05 (5%) is the traditional scientific standard for determining whether given results are statistically significant. A result is expressed as a "p-value," which is a statistical measure of the probability that a difference between groups in a clinical trial happened by chance." (Exh. 1, Am. Compl. ¶ 25.)

the placebo group (p=0.025) and 13% by intent to treat analysis ***(p=0.052)***." (Exh. 16, 12/12/06 Press Release (emphasis added).)

2. The FDA's Refusal To File Hemispherx's First Submission Of The Ampligen® NDA

In August 2006, Hemispherx had its pre-NDA meeting with the FDA, and on December 29, 2006, submitted the pre-clinical section of the Ampligen® NDA to the Agency. (*See* Exh. 2, 2006 Form 10-K at 42.) Hemispherx submitted the entire NDA to the FDA on October 11, 2007. (Exh. 17, 10/11/07 Press Release.) Included in the NDA were the publicly disclosed audited results from the AMP 516 trial, which showed a 0.052 p-value in the intent-to-treat analysis. (*See* Exh. 16, 12/12/06 Press Release.)[27]

On December 5, 2007, Hemispherx received a "refuse to file" letter from the FDA regarding the Ampligen® NDA, which the Company promptly disclosed in a press release, explaining that the FDA had noted "eleven deficiencies . . . in the Clinical Section and three in the Pre-Clinical Section." (Exh. 18, 12/7/07 Press Release.) During an investor conference call hosted by the Company on December 10, 2007, Dr. Carter provided a detailed explanation of these deficiencies, including, *inter alia*, the FDA's concern with cardiac abnormalities seen in CFS patients and whether Ampligen® caused these abnormalities or whether they were caused by the disease itself:

> And the questions by and large turn on the issues of potential cardiac abnormalities. Now this is a very valid question because patients with chronic fatigue syndrome do have certain cardiac and pulmonary abnormalities and the issue is, does it come from the disorder, the sedentary activity, or is it possibly drug induced damage? These are very legitimate questions. Now, 15 years ago

[27] As discussed *infra*, Dr. Carter explained during an interview on May 29, 2009 that these results were further audited during the FDA's review of the Ampligen® NDA, and that this second audit resulted in a final p-value of 0.047, not 0.052. (*See* Exh. 94, 05/29/09 Inter. Tr. at 6.)

> the Commissioner and the division directors selected patients which they selected for special cardiac studies. These are patients who basically had been on Ampligen for a long time, and they requested that studies be done by independent board-certified cardiologists, and a variety of sophisticated studies, including echocardiograms, et cetera, were done. Now remember these were not part of the formal studies and that's, lack of that information is what prompted the reasonable question on the basis of the agency.
>
> Now these studies were conducted; they were conducted in depth. They were reported to the agency, and I should tell you that the results of these studies indicated that none of the patients who were selected by the agency had any abnormalities which could be temporarily [temporally] associated in any way with the drug. And it, and accordingly the Company was permitted to go to phase 2 and ultimately to phase 3. Obviously we did not do this on our own recognizance; we only did it when different reviewers and different associate commissioners approved in writing that we could proceed to the next step. But it, but in any case it is clear now that these documents are effectively too deeply buried in our reports to be readily available to test. And as we sit here this morning, whatever time it is, 9:20, our medical director is highlighting for the agency, as we speak, where these reports are in, within the document production. And again, recognize here you're dealing with tens of thousands of pages of document, and these particular issues that, for example, concern the correspondence of, from the commissioners, were not part of the study reports. These were add-ons, important add-ons which were resolved at the time, to the satisfaction of the agency and to the Company.

(Exh. 69, 12/10/07 Conf. Call Tr. at 4.)

The second category related to "patient accountability." Dr. Carter explained that the FDA was concerned about missing patient files. Dr. Carter reported that the Company would locate those files within the database and point the FDA to the files. (*Id.* at 5.)

Dr. Carter also provided a detailed explanation of the third category of questions raised by the FDA, regarding the validation of endpoints in the Ampligen® clinical trials:

> The agency is asking us to validate the secondary tools that were used to support the treadmill. Now this is in essence a very sophisticated set of statistical questions, where you look at correlation coefficients between patients who did well on the

> treadmill and did they do well in other quality of life, improvements, et cetera. This does not mean new clinical data. It means analyzing in an augmented way the data that you have. Now we have world-class statisticians. In the last year we've had four statistical groups working on this data, including statisticians, senior statisticians formerly at J&J who have presented multi-billion dollar drugs successfully to the advisory committee.
>
> So we know how to do this at the moment that the agency, and we are going to, we plan to meet with them in roughly four weeks. We're going to be sending out the technical response very shortly, within seven to 10 days approximately. But once we're absolutely sure on how they want the correlations to be done, we will move forward very, I believe, very effectively but certainly in a very timely manner to answer those questions.

(*Id.* at 6.)[28]

In addition, Dr. Carter explained that the Company was reviewing its existing data from its studies to gather more evidence of cardiac toxicology to see if the proposed Ampligen® labeling should contain a warning label for cardiac toxicology.

> So not only are we addressing the present issue, but we're going back into the database to make sure that the argument that we have which meets, we feel meets the international harmonization guidelines, that this drug by international harmonization guidelines does not have evidence of cardiac toxicology. We're now looking at the data to see if there are additional ways we can study the database to convince the agency of this or in a, in the alternative, to convince ourselves that perhaps there's a warning. Now we don't believe there's a warning that should be put on a label here.

(*Id.* at 9.)

In a December 19, 2007 investor conference call, Dr. Carter discussed the three issues the FDA had raised regarding the preclinical aspect of the Company's NDA. (Exh. 70, 12/19/07 Conf. Call Tr. at 7.) These issues related to pharmacodynamics (blood levels in

[28] Dr. Carter also explained that the Agency questioned Hemispherx's validation of secondary endpoint in the context of the treadmill testing which also involved "a significant undertaking by our statisticians and by our programmers. But it's a very, very manageable project . . . ." (*Id.* at 8.)

animals) and two additional animal studies one of which would study incidents of carcinogenicity. (*Id.*) Dr. Carter reported that the Company was seeking a waiver of certain pharmacokinetic animal studies and that the FDA had raised concerns about Ampligen®'s carcinogenicity testing. (*Id.*)

> The three questions that we had in the pre-clinical area; the first question involved what's called pharmacodynamics, that is measuring the blood level in animals versus humans. And ironically we did this as early as 1991 and actually found that we had submitted this to the Agency 15 years ago, but as those of you know who've followed the company history, we have been in four, and as I've mentioned in the previous conference call, we've been in four different review divisions, and apparently that particular pharmacokinetic data was missing from the information that was reviewed in our first filing.
>
> Now in addition to this, because the TLR, the TLRs are different between mice and humans, and indeed at the invitation of the Agency based on correspondence we got in May of 2007, a number of companies, including Coley, have been exempted from having to do further pharmacokinetic measurements in animals because it doesn't predict human activity. It doesn't predict human activity because the tissue distribution is different, et cetera. ***And we believe that we will be exempted from further activities on that basis.*** Under the FDA Modernization Act of 1997, the Act clearly states that if one company is exempted from further testing based on certain criteria, that this must uniformly apply to all companies. And any further exemption that we would seek would be based on the precedent that has already been applied to TLR-9, and we also understand was applied to another compound called poly-ICLC, which was used for the treatment of malignant brain cancer in which the company did not have to do pharmacokinetics based upon the relative disparity between TLR-3 in the humans versus the animals. So we believe there is a persuasive position to take here.

(*Id.* (emphasis added).)

Dr. Carter elaborated on the two additional animal studies requested by the FDA, explaining that the FDA did not realize that Hemispherx had already performed two types of animal studies and that if certain conditions were met it would "be convincing evidence" that no

further carcinogenicity studies would be necessary. (*Id.* at 8.) Hemispherx believed that those conditions were met here and therefore it would argue to the Agency that no further carcinogenicity studies would be necessary. As Dr. Carter explained:

> ***Now, the other two questions concerned additional animal studies, in one case to look for additional incidents of carcinogenicity***. We've already done six to nine-month studies for carcinogenicity and we did not see any. And then a request for a second study; apparently the Agency did not yet identify or we did not submit the fact that we've already done two animal studies. We've done both rabbits, which was not recognized yet by the Agency, apparently we misplaced the document, as well as rat. So we've already done two animal settings. But perhaps the most dispositive thing is that we received a statement from the Agency in May, I believe it was May 28, 2007, that if we look at every gene in the human body, which is 30,000 genes, it could be 38,000, but the gene bank right now is about 30 to 35,000. If we looked at every gene in the human body and found that there was no structural relationship between Ampligen structure and these 30 some thousand genes, that that would "be convincing evidence" that there is no need for further carcinogenicity studies. Now originally, by the way, the question was narrowed to about 17 tumor suppressor genes, but more recently it was widened to include 30,000 genes. And I'm pleased to tell you this afternoon that we have done that study, and we will be presenting to the Agency shortly that we have examined 30,000 genes for structural similarity, and we find only two genes, one's called a channel protein gene, it's the gene that has to do with cardiac function, and the other one is an ageneric (sp?) receptor gene which has to do with blood pressure, in which there is slight amology between our drug and that gene. Now neither of these genes have ever been implicated in (inaudible). In fact I'll repeat, neither of these genes has ever been implicated in (inaudible). One gene's been involved in blood pressure, and the other gene is involved in cardiac contractility. ***As a result of the gene that's involved in cardiac contractility, we are expanding our cardiac analysis to include additional cardiac data beyond that required by the international guidelines for harmonization on cardiac function.*** But I think that we will be able to rigorously close the chapter about the potential carcinogenicity of this particular drug vis-à-vis TLR-3 by a survey of, as I said 30 to 35,000 genes. Unfortunately for Coley and for TLR-9, when they did similar studies they found that a tumor suppressor gene wasn't activated. In other words there was a gene that could control dormant cancer, which somehow got

> shutdown by the Coley product. To their credit, by the way, they published this. But I would say that that particular action would make it very challenging to get a compound that would do that, you know, into a clinical setting. Fortunately that situation clearly does not exist with our drug, and we will be submitting all the gene bank data through the Agency so that they can independently verify. And I want to also say that this particular element is one of the, is a sterling work product of Dr. William Mitchell, M.D., PhD. As you know he's a professor (inaudible) pathology at Vanderbilt University, and is the primary architect of this particular study, which is a very, very conclusive study. And I believe a study that will be persuasive to our colleagues at the Agency.

(*Id.* at 7-8 (emphasis added).)

On January 9, 2008, Hemispherx announced that it had formally submitted responses to all fourteen of the FDA's filing questions. (Exh. 19, 01/09/08 Press Release.) On March 6, 2008, the Company issued a press release explaining that nine of the fourteen filing issues were "no longer considered filing-related issues" and that the FDA now only had five filing issues with the NDA. (Exh. 20, 03/06/08 Press Release.) The Company also disclosed that it would address the five remaining issues through a series of five additional amendments to its NDA. (*Id.*) The Company provided details regarding the five remaining issues,[29] and stated that "[i]mportantly, the company believes no further studies are required to achieve a complete NDA filing status for purposes of regulatory review of the entire document." (*Id.*) (emphasis

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[29] The Company explained that the five remaining issues could be grouped into two categories:

> Category (1) Administrative items (four) include: (a) transfers of additional clinical records (termed "CRF's"), (b) transfer of several documents previously submitted to the FDA, (c) additional clinical data reconciliations (compiled from the CRF records) and (d) additional computer generated charts which summarize specific parts of the CRFs. Transfer of these records will thereby allow the Agency reviewers to evaluate independently the statistical efficacy /safety conclusions of the Company's existing NDA. Category (2) (One item): a reformatting and enlarged analysis of the existing pharmacokinetics ("PK") report to more closely align with current International Committee on Harmonization ("ICH") guidelines.

Id.

added). On February 8, 2008, the Company met with the FDA to discuss these amendments. (*See* Exh. 4, 2007 Form 10-K at F-9, 35.)

In March 2008, Hemispherx disclosed that it was conducting stability testing of Ampligen® at both its Hollister-Stier Laboratories facility in Spokane, Washington and at its New Brunswick, New Jersey facility. (Exh. 4, 2007 Form 10-K at 9, 14, 33-34.)

That April, Dr. Carter reported during an investor conference call that the FDA would begin active field audits in the first week of June 2008. (Exh. 71, 04/09/08 Conf. Call Tr. at 2-3.). He also pointed out the FDA had dropped its filing questions about animal testing mentioned in the December 19, 2007 conference call, but, in case the animal questions would continue to be a review issue, the Company was continuing to perform certain studies indicating that animals react differently to Ampligen® than humans and therefore no additional animal studies would be necessary:

> . . . [I]n our initial denial by the agency they said there was some animal question. Now, they took those questions off the board, but in theory, ***those questions may still be existing. And we are addressing that by specific studies that show that the animal response to Ampligen and to TLR-3 is totally different from the human.*** We're making a lot of experimental progress on that working with (inaudible) laboratories.
>
> ***And in the next month or eight weeks we'll be supplementing our application*** and I expect that we will win on this issue that no further animal tests are needed because the animal does not predict the human behavior. So, ***it's an unsettled area of research in a very cautionary agency right now because of the lack of disclosure.*** And like all the other companies in the sector we're paying a little bit of that price by having to especially disclose more underlying documents to make sure that, you know, that we're telling everything. . . .

(*Id.* at 11 (emphasis added).)

On April 25, 2008, Hemispherx addressed the remaining five NDA filing issues by submitting amendments to the NDA. The Company explained that these "amendments

should allow the FDA reviewers to better evaluate independently the statistical efficacy/safety conclusions of our NDA for the use of Ampligen in treating ME/CFS." (Exh. 5, 1Q 2008 Form 10-Q at 12; Exh. 21, 05/13/08 Press Release.)

3. The FDA's Acceptance Of The Amended Ampligen® NDA

On July 8, 2008, the FDA accepted for review Hemispherx's NDA. (Exh. 22, 070/8/08 Press Release.) Although the FDA accepted the NDA as substantially complete for review, Dr. Carter explained in a conference call to investors that "the company is planning to answer certain ***remaining questions*** in the next 10 weeks so that by the end of September we will have – we believe we will have satisfied all the questions. ***Some of you may remember there were earlier questions which were not critical for completeness but that remained*** **important technical questions.**" (Exh. 72, 07/17/08 Conf. Call at 1 (emphasis added).) As explained *supra*, the Company had previously discussed these questions in investor conference calls and press releases.

Although Hemispherx's goal was to submit the new data in the next ten weeks, Dr. Carter explained that the Company had "up to six months" to submit the data. (Exh. 72, 07/17/08 Conf. Call at 2 (emphasis added).) Dr. Carter reported that "the data that we will be completing for the FDA includes ***further data from animal tests and also further analysis of the sera***, which were the samples received from patients who have been in our either well-controlled trials or in our open label trial [AMP 511]." (*Id.* (emphasis added).) He also explained that the Company "[did] not plan any additional clinical trials, although we do have patients on study and ***we are continuing to gather safety and efficacy from those patients who are in our long term trials***." (*Id.* at 2 (emphasis added).)

One investor questioned Dr. Carter about the "outstanding issues with the FDA" including issues with pregnant animals and consult tests with monkeys that may take an additional two years. (*Id.*) Dr. Carter responded:

> ***We do not have a final definitive answer,*** but the reason for our correspondence from the agency indicates that they will accept compelling reasons to not do this. ***We believe we have more than adequate compelling reasons not to do any long term cancer studies and this comes from previous FDA decisions on closely allied drugs.***
>
> So we believe that the correspondence and the history is strongly in our favor.

(*Id.* at 6 (emphasis added).) Recognizing that the Agency might require additional tests anyway, Dr. Carter explained that the Company had a back up plan which was to perform these studies after it received marketing approval:

> Our backup position is to accept to this on a so called conditional basis, where we would do it at the same time we had our marketing approval, we would be creating revenues and we would be reporting these results to the agency as we get them, but it would not interfere with the revenue potential. So that is our backup position but we think that will probably not be necessary based upon the correspondence and based on the history.

(*Id.*)

Dr. Carter then addressed the question of animal toxicology, autoimmune disease, and carcinogenicity testing which he had previously discussed in the December 19, 2007 conference call.

> With respect to your earlier question about with other areas of animal toxicology; ***we are continuing a toxicologic program***. One of the main partners in this is a group in the United States known as the (INAUDIBLE) which is well recognized in this field and with which we've been working for several years. We basically expect those results to be available within the next couple of – next two to three months.

> So we do not see any deterrent to slow down as a result of the preclinical toxicologic program. And obviously I should say, that I made in my introductory remark, ***we're continuing to sample patients as well as animals*** to establish the fact that thus that we have thus far that has never been a single instance of an autoimmune phenomenon which was attributable to this drug. This cannot be stated to my knowledge with any other drug that modulates the immune system.
>
> But because of these very brief pulses of this drug, and an exhausted effort to try to find the low level incidents of rheumatoid arthritis or systemic lupus or other antibodies against internal organs which could stimulate an autoimmune disease; we've absolutely found not a single case within our nearly 1,200 patients, and as you know more than 91,000 clinical observations. ***The other thing that leads us to believe that this issue of carcinogenicity will be retired and its vitality is that the agency has acknowledged that if we fail to see systemic levels of three particular (INAUDIBLE) which are pro-carcinogenic and those happen to be (INAUDIBLE) isle four and isle six according to the FDA that will be a "compelling case" against carcinogenistic.***
>
> And that is exactly the finding that we have. There is no (ph) – that we have not been unable to detect any systemic increase in any of the pro-carcinogenic (INAUDIBLE), and we continue to do this. But all of the results that we have to date are definitely showing no potential to pro-carcinogenic (INAUDIBLE). So we feel comfort – comfortably about this.

(*Id.* at 6-7 (emphasis added).)

In November 2008, Hemispherx reported that it was preparing for "preapproval inspection" by the FDA for the "manufacturing of Ampligen product and its starting materials," and that a "satisfactory recommendation from the FDA Office of Compliance based upon an acceptable preapproval inspection is required prior to approval of the product." (Exh. 7, 3Q 2008 Form 10-Q at 20.) The Company also disclosed that it had engaged Lovelace Respiratory Research Institute in Albuquerque, New Mexico ("Lovelace") "to perform certain animal toxic studies in support of our Ampligen® NDA. ***These studies were requested by the FDA and will be done in collaboration with the resources of the New Brunswick facility. We expect these***

studies to be complete in January 2009." (*Id.*; *see also* 11/18/08 Press Release (announcing the Lovelace studies) (emphasis added).

During a January 29, 2009 interview, Dr. Carter was asked whether additional tests would be needed for the Ampligen® NDA. (Exh. 91, 01.29.09 Inter. Tr. at 9.) Dr. Carter responded that there were additional tests being conducted including animal tests for pre-clinical toxicology and that he anticipated 4-8 weeks to complete those tests. This testing had been previously disclosed by the Company on multiple occasions. Dr. Carter also explained during the January 29 interview that Hemispherx was continuing to accumulate data for the AMP 511 open label study and that it would submit the data to the FDA in connection with the Ampligen® NDA:

> INTERVIEWER: And are there currently additional tests being conducted or will additional tests have to be conducted to add to the NDA already filed for CFS and, if so, how long will they take?
>
> DR. CARTER: There are additional tests which are being conducted, and indeed these include animal tests to round out our preclinical toxicology package. We're projecting perhaps another four to eight weeks to complete those types of tests.
>
> Also, we're continuing to accumulate clinical safety data from our ongoing compassionate or treatment IND program. ***In other words, we're trying to be prepared for any questions which might arise either in the clinical or preclinical area and raised in conjunction with our understanding either of Ampligen, the immune system or the interplay of the immune system and Ampligen with the diagnosis of chronic fatigue syndrome.***

(Exh. 91, 01/29/09 Inter. Tr. at 9-10.)

4. The FDA's Extension Of The February 25, 2009 PDUFA Date

On February 18, 2009, Hemispherx announced that the FDA had extended the Ampligen® NDA PDUFA date from February 25, 2009 to May 25, 2009. (Exh. 24, 02/18/09

Press Release.) The Company explained that the reason for the three month extension was to "***provide time for a full review of [the Company's recent] submission.***" (*Id.*)

Dr. Carter further clarified the reason for the PDUFA date extension during a February 22, 2009 interview. He explained that the FDA extended the date because the Company had submitted additional data to the FDA within 90 days of the PDUFA date, and that the data related to why patients with CFS have a higher incidence of catastrophic heart disease. (Exh. 92, 02/22/09 Inter. Tr. at 7-10.) In response to the interviewer's questions, Dr. Carter provided detailed information about these data:

> INTERVIEWER: So the PDUFA date was extended until May 25th because additional information was filed. Now, how come the company didn't have that data much earlier?
>
> DR. CARTER: In our new filing we examined a detailed analysis of over 1,000 sufferers with chronic fatigue syndrome and over 1,000 electrocardiograms, trying to look for long- term trends that might explain why these patients have a higher incidence, for example, of catastrophic heart disease. Why do they have heart attacks which kill them? Why do they have heart failure?
>
> And in the analysis of this long-term data, which has only been available to us really in the last month or so, we found important clues which we believe give new insight into the sudden death of patients with chronic fatigue syndrome.
>
> Remember that they, that they typically acquire the disease in the age of 38 to 41, relatively young people. Females, females of course tend to have a cardioprotective effect because of the estrogens that they have, so why are they dying at these earlier ages?
>
> And we believe that we have discovered an important new, new reason for this and that Ampligen may be able to mitigate some of these deaths. And that's going to be the basis of the presentation that will be made in a couple of weeks at the International Chronic Fatigue Syndrome meeting.
>
> * * * * *

> INTERVIEWER: And I understand that you cannot go into much detail until the information is presented to a scientific forum. But in general can you explain the importance of this data to us?
>
> DR. CARTER: Well, in general we have examined the major causes of death in chronic fatigue syndrome. And the major causes of death include heart failure, suicide and cancer.
>
> And we have looked back over our data, including the data from the earlier 502 study, which was a well controlled, placebo controlled study, as well as our more recent well controlled study, and we have reached certain information which, while we can't go into the details of it at this, today, prior to the conference, we can say that the patients with chronic fatigue syndrome, having so many severe symptoms, take many medications -- we call these concomitant medications -- for controlling the symptoms of the disease.
>
> And we have found that in the drug, in the group that takes Ampligen there is a reduction in these concomitant medications.
>
> Unfortunately, some of these medications which the patients are taking alter the electrocardiogram in such a way that it predisposes the person to heart failure or heart attack. And, fortunately, in the setting of taking Ampligen we were able to demonstrate that there is a statistically significant reduction in these drugs which are potentially very harmful to the patient and which potentially could be life-threatening.

(*Id.* at 8-9, 10-11.)

In its 2008 Form 10-K, filed on March 16, 2009, Hemispherx updated investors on the status of the Lovelace animal toxicology studies that were being conducted in support of the Ampligen® NDA. (Exh. 8, 2008 Form 10-K at 25, 81.) The Company had previously disclosed these studies in its third quarter 2008 Form 10-Q, filed on November 10, 2008. (*See* Exh. 7, 3Q 2008 Form 10-Q at 20.)

In addition, Hemispherx reported on the FDA's nine-day preapproval inspection of the Company's New Brunswick facility in January-February 2009, which resulted in a Form 483 citing Hemispherx's "need to re-perform four method validations." (Exh. 8, 2008 Form 10-

K at 25.) The Company also reminded investors that the FDA had conducted a field investigation in its Spokane, Washington facility in June and July 2008 and that that inspection also had resulted in a Form 483. (*Id.*) Hemispherx had previously disclosed these "infractions" during the July 17, 2008 investor conference call. (*See* Exh. 72, 07/17/08 Conf. Call at 7.)

In its Form 10-K, the Company cautioned investors that, due to increased workloads at the FDA and the possible impact of the recently enacted and implemented FDA Amendments Act and Safety First/Safe Use initiatives, the Agency may not have sufficient time to complete a full review of the recently submitted data and reach a decision on the Ampligen NDA by May 25, 2009. (*Id.* at 89.)

On March 19, 2009 Hemispherx conducted an investor conference call in which the company provided additional detail on the status of its NDA. The Company began by explaining that they were "***continuing to provide brief reports, especially on animal data, to the Agency as has been requested***." (Exh. 73, 03/19/09 Conf. Call Tr. at 2 (emphasis added).)

Dr. Carter then explained that Hemispherx:

> Continue[s] to provide what I would call small residual data chunks to the Agency which compare and contrast our product with the spectrum of other TLRs which have been placed into clinical trials. These obviously not only concerned how they work, but they especially concern issues about product safety and unintended consequences, which have been the possible downfall of a number of these products and which to date we have been able to demonstrate that these unintended consequences have not been observed with our product. We feel very positive about that.

(*Id.* at 3.)

In addition, Dr. Carter updated investors on the status of the two Form 483s issued to the Spokane and New Brunswick facilities explaining that it expected to resolve the issues at the New Brunswick facility in the first part of April.

> We noted in the K that the New Jersey district office of the FDA had conducted about a nine-day inspection in January and early February of this year of our New Jersey facility. We were very pleased to note that we had less than one page of infractions; typically these may be 25 to 100 pages in length. We noted in the K that we had four method validations which needed to be done. This basically involved equipment that had been moved from our facility in Rockwell, Maryland, to the New Brunswick location. In the determination of the inspector, this equipment needed to be revalidated. In the K, we actually estimated that this might take up to three months to do. But I am pleased to announce today that we have shortened that period to about two weeks, and we expect to respond definitively to the FDA inspection in the first part of April. So we are very pleased to make that announcement.

(*Id.* at 2.) The Company had previously reported the Form 483 in its 2008 Form 10-K. (Exh. 8, 2008 Form 10-K at 35.) It also provided an update regarding the FDA's field inspection of the Spokane, Washington facility:

> We also noted in the K that the FDA had conducted a field inspection at Hollister-Stier Laboratories in Spokane, Washington, in mid-2008 -- actually between June 19 and July 2, 2008. They noted several observations under what we call final fill operations which were not in compliance with the federal regulations. These were basically variations in the process of filling the vials.

(*Id.* at 2.) The Company had previously disclosed these issues during the July 17, 2008 investor conference call and in the 2008 Form 10-K filed on March 16, 2009. (Exh. 72, 07/17/08 Conf. Call. Tr. at 7; Exh. 8, 2008 Form 10-K at 35.)

During the March 19 conference call, Dr. Strayer reported on the Company's pro-inflammatory cytokines research, and discussed the QT study data that Hemispherx had submitted to the FDA in January. (Exh. 73, 03/19/09 Conf. Call. Tr. at 6-7.) A conference call participant asked about the May 25, 2009 PDUFA date to which Dr. Carter responded that the Company "believe[d] that [it] ha[d] answered all the major questions" from the FDA but that the Agency could "***continue*** to ask questions as long as they want." (*Id.* at 12 (emphasis added).) Dr. Carter went on to explain that Hemispherx was "trying to anticipate questions that might

come up in the future so that [it] [could] be prepared should there be further questions." (*Id.*) When asked what he thought was the likelihood of FDA approving the Ampligen® NDA, Dr. Carter reiterated that "all we can do is cite historically data because obviously no one can read the future." (*Id.* at 14.)

On May 11, 2009, Hemispherx reported that the four method validations that needed to be re-performed at the New Brunswick facility as noted in the Form 483 "have been completed and the reports were forwarded to the FDA on April 28, 2009 for review." (Exh. 9, 1Q 2009 Form 10-Q at 18.) The Company also provided an update on the final fill issues relating to "two observations dealing with reviews and validations of process variability" at the Spokane, Washington facility. Hemispherx reported that it was "continu[ing] to work with Hollister-Stier to finalize specific actions to address the FDA Form 483 issues and Hollister-Stier has submitted a specific action plan to the Seattle, Washington office of the FDA." (*Id.* at 22.) Finally, the 2008 Form 10-K provided an update on the Company's progress on the Lovelace animal toxicology studies, explaining that it "expect[ed] these studies to be complete in mid-2009." (*Id.* at 35.)

When asked about the status of the animal studies during May 15, 2009 interview, Dr. Carter explained: "[W]e have completed the animal studies that were requested by the agency and we have . . . produced an initial report of the studies, and now we are in the process of submitting final reports. But we've already given the conclusions to the agency in brief but substantive animal reports." (Exh. 93, 05/15/09 Inter. Tr. at 8.) He also discussed the newly discovered cardiac data that was submitted to the Agency in January 2009 and which Dr. Strayer discussed in the March 19, 2009 conference call. (*Id.* at 13-15.) Dr. Carter reported that the Company believed that the data would help explain why CFS patients have increased

cardiovascular events. While Dr. Carter was "encouraged" by the data, he also reported that "obviously this is all subject to FDA analyzing [the data] themselves." (*Id.* at 11-15.)

Dr. Carter reaffirmed that while the Company is "encouraged" about the prospects for approval of Ampligen, the Company "also know[s] that there could be a delay because of issues that might arise. Obviously, the regulatory agencies worldwide are very much concerned about drug safety and drug efficacy, perhaps more so than ever." (*Id.* at 20-22.) Dr. Carter acknowledged that the Company would need "further dialogue with the agency about some of these recently discovered data." (*Id.*)

In May 2009, the FDA advised the Company that due to "certain staffing scheduling changes" the Agency may require "up to 1-2 additional weeks to take action beyond" the PDUFA date of May 25, 2009. (Exh. 35, 05/26/09 Press Release.) The Company reported that the FDA "did not request additional information from the Company at this time." (*Id.*)

During a May 29, 2009 interview, Dr. Carter was asked whether the intent-to-treat results from the AMP 516 Phase 3 trial showed statistical significance. Dr. Carter explained that the data had been audited in connection with the FDA's review of the Ampligen® NDA and that as result of that audit, the p-value was 0.047 and, therefore, was statistically significant according to the FDA's 0.050 criterion. (Exh. 94, 05/29/09 Inter. Tr.) Dr. Carter also confirmed that the 0.047 p-value was the number that had been submitted to the FDA:

> Mr. Vlaicu: So this 0.0472 [sic] is indeed [the] number which was submitted to the FDA.
>
> Dr. Carter: That was the final number from all the patients with the, with the audited data. That's correct.

(Id. at 6.)

On June 12, 2009, during an interview, Dr. Carter reported that Hemispherx had not yet heard from the FDA, which had missed the May 25 PDUFA deadline for making a

decision on the Ampligen® NDA. (Exh. 95, 06/12/09 Inter. Tr. at 2-3.) During a June 22, 2009 investor conference call, Dr. Carter again reported that the Company had not received any news from the FDA but that it was ***continuing*** to provide "complete audited reports on a variety of safety issues that the Agency has raised over the years." (Exh. 74, 06/22/09 Conf. Call. Tr. at 5 (emphasis added).)

Dr. Carter also explained that Hemispherx was "***regularly*** providing reports to the Agency to different reviewers in different areas, for example in the area of preclinical toxicology." (*Id* at 9 (emphasis added).) In response to a question about whether the FDA was awaiting any more data or documents from the Company, Dr. Carter explained that it was hard for Hemispherx to determine what the Agency will consider material but that he did not "think there [were] any documents" outstanding. (*Id.* at 9.)

On August 10, 2009, Hemispherx filed its second quarter 2009 Form 10-Q and in that report provided an update on the Forms 483 that had been issued to the Brunswick, New Jersey and Spokane, Washington facilities, and a status report on the Lovelace animal toxicology studies. (Exh. 10, 2Q 2009 Form 10-Q at 22.) As for the Form 483 that was issued to the New Brunswick facility, the Company explained that "[t]he validations have been completed and the reports were forward to the FDA on April 28, 2009 for review. As a result, the New Jersey office of the FDA has indicated that there are no more preapproval review issues at this time." (*Id.* at 22.) With regard to the reviews and validations of process variability cited at the Hollier-Stier facility in Spokane, Washington, Hemispherx reported that it would "continue to work with Hollister-Stier to finalize specific actions to address the FDA Form 483 issues and Hollister-Stier has submitted a specific action plan to the Seattle, Washington office of the FDA. It is our

expectation that these issues will be resolved and we will be able to complete the resultant sequential validations ***by the end of 2009***." (*Id.* (emphasis added).)

As for the animal toxicology studies, the Company reported that the "studies have been substantially completed with summary reports expected to be issued to the FDA ***during the third quarter of 2009***. Data for final FDA reports are presently undergoing internal auditing at Lovelace and Hemispherx with a projected completion of the final report for late 2009 to early 2010." (*Id.* (emphasis added).)

During a September 9, 2009 investor conference call, Dr. Carter reported that the Company still had not heard from the FDA regarding its Ampligen® NDA. (Exh. 75, 09/11/09 Conf. Call Tr. at 5.) Adam Feuerstein, a columnist for TheStreet.com financial blog, participated in the conference call and Feuerstein questioned Dr. Carter about his communications with the FDA:

> Q – Adam Feuerstein: Can you tell [ph] – when was the last time you had any contact with the FDA regarding the ampligen – the ampligen application?
>
> A – William Carter: ***We – I would say yesterday, we provided an annual report on both of these products yesterday. Annual reports basically look at the clinical activity, any adverse events.***
>
> Q – Adam Feuerstein: But when did you have an actual conversation with someone at the FDA? In the office the FDA that is reviewing ampligen specifically. Did you, I mean when was the last time you've had a conversation where you called them said, hey, what's going on with the review?
>
> A – William Carter: We have not called them and asked that question. We do have – I think I might have described this in that recent conference call. ***We have regular interactions with reviewers providing documents. Essentially, these have been documents in the pre-clinical safety issue. We forward documents, if they have questions, they send back.***
>
> Q – Adam Feuerstein: Since you've met, you've not – no one, Hemispherx has called FDA and said, you were supposed to give

> [Inaudible] on May 25 and it's now September 9? You never had – you never called them?
>
> A – William Carter: ***No, it's – it's our belief that a) in the good space of time, the FDA will respond to us much like they do with all other companies. And in the meantime, we are cleaning up, so to speak, and this is obviously jargonese, certain open issues that are related to the pre-approval inspection of the drug. [Inaudible]. Any other questions?***

(*Id.* at 6 (emphasis added).)

During an October 9, 2009 interview, Dr. Carter reported on the status of the Lovelace animal toxicology studies in response to questions about Hemispherx's communications with the FDA about the status of the Ampligen® NDA:

> Q. We have been contacted by so many members of the investment community who have asked us to contact you in regards to whether or not there has been communication between your company and the FDA about this -- the status of that drug application.
>
> A. Well, as I've noted, at some of the recent health care conferences ***we continue to be in contact with the agency concerning certain requests that they have made to us over the last year that have to do with what we call toxicology***.
>
> This is non-clinical work on the drug which is customarily part of the new drug application. ***So we've continued to complete reports and we expect sometime this quarter, the fourth quarter, to complete a set of requirements that have to do with clinical -- sorry -- pre-clinical toxicology.***
>
> Now, in addition to that, the agency has done a number of audits of our clinical sites as well as our manufacturing facility over the last 12 months. I'm very pleased to say the clinical inspections resulted in no findings which required corrective action by the company, which I believe is a very unusual positive result given the complexity and the duration of our clinical studies.

(Exh. 96, 10/09/09 Inter. Tr. at 8-9 (emphasis added).)

Dr. Carter also provided an update regarding the status of the two Form 483s that had been issued in connection with the FDA's inspections of Hemispherx's New Brunswick, New Jersey and Spokane, Washington facilities.

> [T]he agency did note certain compliance issues at our facility in New Brunswick, which we own, and also at a contract laboratory in Spokane, Washington where we do something called fill and finish. We put the Ampligen into the final container.
>
> Now, ***over the summer of 2009*** we remediated the small compliance issues that existed in our own facilities and we submitted it to the regional office of the FDA, which is in New Jersey.
>
> At the present time ***we are about to complete the remediation as we see it in the contract laboratory in Spokane***. I believe that ***in the next several weeks that work will be completed*** and that will then generate a report to the regional office of the agency, which is in Seattle, I believe.
>
> ***Now, until all those reports are completed and filed satisfactorily with the agency, the agency can withhold a final decision on the commercialization of the product.*** But we believe that we will have achieved everything, to the best of our knowledge, which is necessary for the completion of what we call pre-approval inspections by the agency. So we would expect that any time thereafter to receive final comments from the FDA.

(*Id.* at 9-13 (emphasis added).

In November 2, 2009, Hemispherx issued a press release summarizing the recent reports the Company had submitted to the FDA over the course of the year and the data it planned on submitting in the next couple of months, including data from the Lovelace animal toxicology studies, and the final validation reports relating to the manufacturing issues cited in the FDA Form 483 issued to the Spokane, Washington facility:

> The Company also plans to complete all outstanding queries from the FDA regarding its New Drug Application (NDA) for Ampligen®, an experimental therapeutic, during November and December, 2009. On May 26, 2009, the Company announced a delay on the Ampligen NDA which, at the time, had a PDUFA

> date of May 25, 2009. As noted in the 10-Q and 10-K filings at the time, the FDA did not request additional information from the Company at that time. ***However, several outstanding NDA items, requiring Hemispherx responses, existed at the time of the FDA delay as noted in the August 8, 2009, 10Q filing.*** Between March 9, 2009 and September 15, 2009, the Company issued six (6) new reports to the Agency spanning various subjects including a) clinical safety assessments, b) specialized pre-clinical toxicology reports, and c) abbreviated chemistry and manufacturing control reports. The Company believes that these reports may fully retire all Agency queries in these particular areas.
>
> The Company also plans to submit four (4) additional reports on interrelated topics in November and December, 2009, which will include pharmacokinetic analyses in multiple lower animal species (primates, rodents, etc.) ("the Lovelace Laboratory Studies") and final validation reports of certain manufacturing procedures conducted at an independent facility, Hollister-Stier Laboratories in Spokane, WA. Some of these reports were recently cited in BioMedReports.com and the Science Business Exchange (October 15, 2009).

(Exh. 58, 11/02/09 Press Release.)

As discussed *supra*, Hemispherx previously advised investors of the existence of ***all*** the matters referenced in the November 2 press release.

First, the Company provided investors with regular updates on the status of the animal toxicology testing that was underway at Lovelace. This testing was discussed in the December 19, 2007 investor conference call; the March 6, 2008 press release; the April 9, 2008 investor conference call; the July 17, 2008 investor conference call; January 29, 2009 interview of Dr. Carter; the third quarter 2008 Form 10-Q; 2008 Form 10-K;, 2009 interview conference call; the March 19, 2009 investor conference call; the 2009 Q1 Form 10-Q; May 15, 2009

interview; the July 22, 2009 investor conference call, the second quarter 2009 Form 10-Q; and the October 9, 2009 interview of Dr. Carter.[30]

Second, the Spokane, WA inspection issues were disclosed on numerous occasions as well: in the July 17, 2008 investor conference call; the 2008 Form 10-K; March 19, 2009 investor conference call; first quarter 2009 Form 10-Q; July 22, 2009 investor conference call; the second quarter 2009 Form 10-Q; and the October 9, 2009 interview. The company also disclosed the same progress in its Q3 Form 10-Q (filed 11/9/09). See Q3 Form 10-Q at 16 (filed 11/9/09).[31]

5. The FDA's Complete Response Letter

On December 1, 2009 Hemispherx issued a press release announcing that the Company had received a Complete Response Letter from the FDA. (Exh. 62, 12/1/09 Press Release.) As the press release explained, in accordance with Complete Response procedures, "the FDA reviewers determined that they cannot approve the application in its present form and provided specific recommendations to address the outstanding issues." (*Id.*)

Specifically, the Complete Response Letter indicated that:

> that the two primary clinical studies submitted with the NDA did not provide credible evidence of efficacy of Ampligen® and recommends at least one additional clinical study which shows a convincing effect and confirms safety in the target population. The FDA indicated that the additional study should be of sufficient size and sufficient duration (6 months) and include appropriate monitoring to rule out the generation of autoimmune disease. In

[30] *See* Exh. 70, 12/19/07 Conf. Call. Tr. at 6; Exh. 20, 03/06/08 Press Release; Exh. 71, 04/09/08 Conf. Call Tr. at 11; Exh. 72, 07/17/08 Conf. Call. Tr. at 6-7; Exh. 7, 3Q 2008 Form 10-Q at 20; Exh. 8, 2008 Form 10-K at 35.; Exh. 91, 01/29/09 Inter. Tr. at 9; Exh.73, 03/19/09 Conf. Call Tr. at 2; Exh. 9, 1Q 2009 Form 10-Q at 18; Exh. 93, 05/15/09 Inter. Tr. at 8; Exh.92, 02/22/09 Inter. Tr. at 9; Exh. 10, 2Q 2009 Form 10-Q at 22; Exh. 96, 10/09/09 Inter. Tr. at 10-11.

[31] *See* Exh. 72, 07/17/08 Conf. Call. Tr. at 7; Exh. 8, 2008 Form 10-K at 35.; Exh. 9, 1Q 2009 Form 10-Q at 18; Exh. 10, 2Q 2009 Form 10-Q at 22; Exh. 96, 10/09/09 Inter. Tr. at 9.

> addition, patients in the study should be on more than one dose regimen, including at least 300 patients on dose regimens intended for marketing. ***Finally, the additional study must incorporate both a well-controlled QT interval study and pharmacokinetic evaluations.***
>
> Other items required by the FDA include certain aspects of Non-Clinical safety assessment, and Product Quality. ***In the Non-Clinical area, the FDA is recommending that the Company complete rodent carcinogenicity studies in two species. As part of the NDA submission, the Company had requested that these studies be waived, but the waiver has not been granted. Certain additional non-clinical studies and additional data to support non-clinical studies already submitted with the NDA are also recommended by the FDA. Prior to the receipt of the Complete Response letter, the Company had already begun many of these additional studies and the collection of the requested additional data.***
>
> Under the Product Quality section of the Complete Response letter, the FDA recommends that the Company submit additional data and complete various analytical procedures. The collection of these data and the completion of these procedures is already part of the Company's ongoing Quality Control, Quality Assurance program for Ampligen® manufacturing under cGMP (current Good Manufacturing Practice Guidelines) and the manufacturing enhancement program recently undertaken by the Company and announced in a news release on September 16, 2009.
>
> Finally, the FDA commented on Ampligen® manufacturing noting the need to resolve outstanding inspection issues at the facilities producing Ampligen®. These include the Company facility located in New Brunswick, NJ and one of the Company's third party manufacturing facilities (Hollister-Stier Laboratories). The Company has been working to resolve these issues.

(*Id.* (emphasis added).)

As discussed *supra*, Hemispherx repeatedly reported to the market – throughout the putative Class Period – that it was conducting pre-clinical (animal) toxicology studies. The Company also advised investors during the July 17, 2008 conference call that it had sought a waiver of the FDA's carcinogenicity testing requirement, and the Company discussed the

carcinogenicity issue during the December 19, 2007 and April 9, 2008 conference calls as well.[32] At no time did Hemispherx guarantee that the Agency would grant its waiver request.

In addition, the Company previously disclosed that it had submitted QT data to the FDA in January 2009, thereby making it clear that the FDA considered the QT interval analyses to be relevant to the Ampligen® NDA. (*See* Exh. 73, 03/19/09 Conf. Call. Tr. at 7.) Hemispherx did not, however, make any guarantees that the FDA would consider the Company's QT data to be sufficient. Nor has plaintiff pleaded any facts suggesting that the Company somehow ***knew*** in advance that the FDA would require a second QT interval study.

Finally, the FDA would not have accepted the Ampligen® NDA for filing had it believed Hemispherx's Phase 3 data, on their face, failed to show "credible evidence of efficacy." Indeed, had the Company's data so ***clearly*** failed to show efficacy – as plaintiff avers (*see* Exh. 1, Am. Compl. ¶ 58) – then the FDA would have refused to conduct a substantive review of the NDA. (*See supra* Section II.A.2 (FDA may refuse to accept NDA for filing where there is a "clear failure to include evidence of effectiveness compatible with the statute and regulations" (citation omitted).)

As this chronology of Hemispherx's public statements regarding the Ampligen® NDA before and during the putative Class Period amply demonstrates, defendants promptly and fully disclosed the very information plaintiff claims they misleadingly omitted. As explained in Section IV.A below, defendants' detailed and transparent disclosures completely undermine plaintiff's ability to allege a misstatement or omission of material fact, much less a strong inference of scienter.

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[32] *See* Exh. 71, 04/09/08 Conf. Call Tr. at 11; Exh. 70, 12/19/07 Conf. Call Tr. at 7-8; Exh. 72, 07/17/08 Conf. Call Tr. at 7.

III. APPLICABLE PLEADING STANDARDS

Because plaintiff's Amended Complaint seeks relief for alleged federal securities fraud under Section 10(b) of the Securities Exchange Act of 1934 ("Exchange Act'), 15 U.S.C. §78j(b), and Rule 10b-5, 17 C.F.R. §240.10b-5, promulgated by the Securities and Exchange Commission ("SEC"), the Court must determine, not only whether plaintiff's allegations state a claim upon which relief can be granted under Federal Rule of Civil Procedure 12(b)(6), but also whether the averments comply with the heightened pleading requirements of the PSLRA, which has replaced Rule 9(b) as the pleading standard for private Rule 10b-5 actions. *See Institutional Investors Group v. Avaya, Inc.*, 564 F.3d 242, 253 (3d Cir. 2009). Both Rule 12(b)(6) and the PSLRA require that the Court "'consider the complaint in its entirety, as well as documents incorporated into the complaint by reference, and matters of which a court may take judicial notice.'" *Avaya*, 564 F.3d at 252 (quoting *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, 551 U.S. 308, 322 (2007)).

A. Complaints Whose Factual Allegations Fail To Raise A Right To Relief Above The Speculative Level Must Be Dismissed Under Rule 12(b)(6)

To survive a motion to dismiss under Rule 12(b)(6), a complaint must plead "enough facts to state a claim to relief that is plausible on its face." *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 570 (2007).[33] Thus, factual allegations that fail "to raise a right to relief above the speculative level" or merely state a "conceivable" claim will not suffice. *Id.* at 555, 570. And though a court must accept as true a complaint's well-pleaded factual allegations and draw all reasonable inferences therefrom in the light most favorable to the plaintiff, *Nami v. Fauver*, 82

[33] *See also Ashcroft v. Iqbal*, 129 S. Ct. 1937, 1953 (2009) (confirming that pleading standards delineated in *Twombly* apply to all civil actions).

F.3d 63, 65 (3d Cir. 1996), it need not give credence to "bald assertions" or "legal conclusions," *In re Burlington Coat Factory Sec. Litig.*, 114 F.3d 1410, 1429 (3d Cir. 1997), or "sweeping legal conclusions cast in the form of factual allegations," *Morse v. Lower Merion School Dist.*, 132 F.3d 902, 906 n.8 (3d Cir. 1997).

B. The PSLRA Mandates The Dismissal Of Complaints That Fail To Comply With Its Heightened Pleading Requirements

All complaints seeking relief under the federal securities laws must satisfy the PSLRA's "stringent" pleading requirements, which were intended by Congress to "curtail the filing of meritless lawsuits." H.R., No. 104-369, at 41 (1995) (Conf. Rep.), *reprinted in* 1995 U.S.C.C.A.N. 730, 740. *See, e.g.*, *In re Advanta Corp. Sec. Litig.*, 180 F.3d 525, 531 (3d Cir. 1999) (citing H.R., No. 104-369, at 37 (1995) (Conf. Rep.), *reprinted in* 1995 U.S.C.C.A.N. 730) (noting the PSLRA is designed to limit: "(1) the practice of filing lawsuits against issuers of securities in response to any significant change in stock price, regardless of defendants' culpability; (2) targeting of 'deep pocket' defendants; (3) the abuse of the discovery process to coerce settlement; and (4) manipulation of clients by class action attorneys.").

Specifically, the PSLRA imposes on plaintiffs asserting securities law violations "two distinct pleading requirements, both of which must be met in order for a complaint to survive a motion to dismiss." *Institutional Investors Group v. Avaya, Inc.*, 564 F.3d 242, 252 (3d Cir. 2009). First, the complaint must "specify each allegedly misleading statement" and "why the statement was misleading, and, if an allegation is made on information and belief, all facts supporting that belief with particularity.'" *Id.* at 252-53 (construing 15 U.S.C. § 78u-4(b)(1)) (case citation and internal quotation marks omitted). Where, as here,[34] a plaintiff's "allegations

[34] *See* Exh. 1, Am. Compl. ¶ 1.

are made on information and belief, the complaint must not only state the allegations with factual particularity, but must also describe the sources of information with particularity, providing the who, what, when, where and how of the sources, as well as the who, what, when, where and how of the information those sources convey. *Id.* at 253.

Second, the complaint must, "'with respect to each act or omission alleged to violate this chapter, state with particularity facts giving rise to a strong inference that the defendant acted with required state of mind.'" *Id.* at 253 (quoting 15 U.S.C. § 78u-4(b)(2)). For Rule 10b-5 actions, the required state of mind is scienter – "the defendant's intention 'to deceive, manipulate, or defraud.'" *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, 551 U.S. 308, 319 (2007) (quoting *Ernst & Ernst v. Hochfelder*, 425 U.S. 185, 194 & n.12 (1976), and citing 15 U.S.C. § 78u-4(b)(1), (2) (2007)).[35]

Where, as here, a complaint fails to comply with the PSLRA's heightened pleading requirements, "the court ***shall***, on the motion of any defendant, dismiss the complaint . . . ." 15 U.S.C. § 78u-4(b)(3)(A) (2007) (emphasis added). Indeed, the Third Circuit has consistently upheld the dismissal of federal securities fraud claims that fail to meet the PSLRA's heightened pleading requirements.[36]

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[35] Although the "with particularity" language of the PSLRA "echoes precisely Fed. R. Civ. P. 9(b)" and therefore "requires plaintiffs to plead the who, what, when, where and how: the first paragraph of any newspaper story," the PSLRA's standard for pleading scienter "marks a sharp break with Rule 9(b)," as the plaintiff must plead the defendant's state of mind, *i.e.*, scienter, "with particularity" and not "generally." *Avaya*, 564 F.3d at 253 (quotation marks and internal citations omitted.) *See infra* Section V.E for a more detailed discussion of the PSLRA's heightened requirements for pleading scienter.

[36] *See Investors Group v. Avaya, Inc.*, 564 F.3d 242 (3d Cir. 2009); *In re Discovery Labs Sec. Litig.*, 276 Fed.Appx. 154 (3d Cir. 2008); *Winer Family Trust v. Queen*, 503 F.3d 319 (3d Cir. 2007). *Key Equity Investors, Inc. v. Sel-Leb Mktg. Inc.*, 246 Fed. Appx. 780 (3d Cir. 2007); *Globis Capital Partners, L.P. v. Stonepath Group, Inc.*, 241 Fed. Appx. 832 (3d Cir. 2007); *In re Merck & Co., Inc. Sec. Litig.*, 432 F.3d 261 (3d Cir. 2005); *Klein v. Autek Corp.*, 147 Fed. Appx. 270 (3d Cir. 2005); *Cal. Public Employees' Ret. Sys. v. Chubb Corp.*, 394 F.3d 126 (3d Cir. 2004); *In re Great Atl. & Pac. Tea Co., Inc. Sec. Litig.*, 103 Fed. Appx. 465 (3d Cir. July 9, 2004); *In re Alpharma Inc. Sec. Litig.*, 372 F.3d 137 (3d Cir. 2004); *GSC Partners CDO Fund v. Wash.*, 368 F.3d 228 (3d Cir. 2004); *In re Digital Island Sec. Litig.*, 357 F.3d 322 (3d Cir. 2004); *Hemphill v. Meyerson*, 65 Fed. Appx. 776 (3d Cir. 2003); *In* (continued...)

C. When Deciding A Motion To Dismiss Under Rule 12(b)(6) And The PSLRA, A Court May Consider Documents That Are Integral To The Complaint And Matters Of Which It May Take Judicial Notice

In assessing whether a Rule 10b-5 complaint complies with the PSLRA's pleading requirements, a court "must consider the complaint in its entirety, as well as other sources courts ordinarily examine when ruling on Rule 12(b)(6) motions to dismiss, in particular, documents incorporated into the complaint by reference, and matters of which a court may take judicial notice." *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, 551 U.S. 308, 322 (2007). Accordingly, when deciding a motion to dismiss a Rule 10b-5 complaint, a court may consider any "document[s] integral to or explicitly relied upon in the complaint" without converting the motion into a motion for summary judgment. *In re Rockefeller Ctr. Props., Inc. Sec. Litig.*, 184 F.3d 280, 287 (3d Cir. 1999) (citations omitted).[37] The Court also may consider other publicly available documents, such as the full text of a defendant company's SEC filings, press releases, investor conference call transcripts, newspaper articles and stock price data not specifically referenced in the complaint. *See, e.g., In re NAHC, Inc. Sec. Litig.*, 306 F.3d 1314, 1331 (3d Cir. 2002) (reviewing three separate categories of documents: (1) documents relied upon in the complaint (company SEC filings and press releases); (2) documents filed with the SEC, but not relied upon in the complaint; and (3) stock price data compiled by the Dow Jones news service); *Cal. Pub. Employees' Ret. Sys. v. Chubb Corp.*, No. 00-4285, 2002 U.S. Dist. LEXIS 27189, at

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(continued...)

re Rockefeller Ctr. Props., Inc. Sec. Litig., 311 F.3d 198 (3d Cir. 2002); *In re NAHC, Inc. Sec. Litig.*, 306 F.3d 1314 (3d Cir. 2002); *Oran v. Stafford*, 226 F.3d 275 (3d Cir. 2000); *In re Advanta Corp. Sec. Litig.*, 180 F.3d 525 (3d Cir. 1999); *In re Burlington Coat Factory Sec. Litig.*, 114 F.3d 1410 (3d Cir. 1997).

[37] Here, plaintiff states that the allegations of the Amended Complaint are based on, *inter alia*, the review and analysis of "filings made by Hemispherx with the SEC; . . . press releases, public statements, news articles, securities analysts' reports and other publications disseminated by or concerning Hemispherx; . . . other publicly available information about Hemispherx." (Exh. 1, Am. Compl. ¶ 2.)

*35-40 (D.N.J. June 25, 2002) (taking judicial notice of news articles and transcripts of investor conference calls); *In re Discovery Labs Sec. Litig.*, No. 06-1820, 2006 U.S. Dist. LEXIS 79823, at *23 n.12, *33 n.21, and *34 (E.D. Pa. Nov. 1, 2006) (taking judicial notice of news articles, press releases, and investor conference call transcripts).

In addition, the Court may properly consider publicly available documents issued by government agencies, such as guidance manuals that are available on the website of the FDA. *See, e.g., Noble Asset Mgmt. v. Allos Therapeutics, Inc.*, No. 04-CV-1030, 2005 U.S. Dist. LEXIS 24452, at *7-8 (D. Colo. Oct. 20, 2005) (denying plaintiff's motion to strike FDA guidance documents and explaining that public documents related to the FDA's "process for reviewing new drug applications and that process is central to an evaluation of the claims made in this case"); *DeMarco v. DepoTech Corp.*, 149 F. Supp. 2d 1212, 1218-19 (S.D. Cal. 2001) (recognizing that, on motion to dismiss, court may properly consider transcript of FDA advisory committee meeting), *aff'd*, No. 01-55298, 32 Fed. Appx. 260 (9th Cir. 2002).

Also, a court may even review published articles that are not cited in or otherwise integral to a complaint so long as it considers the articles, "not for the truth of the matters asserted therein, but rather merely to note and acknowledge that the existence of those documents and what they contain about relevant matters at relevant times may serve other legitimate purposes in the Court's consideration of the motions before it." *In re Alstom SA Sec. Litig.*, 406 F. Supp. 2d 402, 408-09 (S.D.N.Y. 2005) (citing cases).

Finally, "[t]he Court need not accept as true any allegations that are contradicted by documents deemed to be part of the complaint, or materials amenable to judicial notice." *In re Yukos Oil Co. Sec. Litig.*, No. 04-CV-5243, 2006 U.S. Dist. LEXIS 78067, at *35 (S.D.N.Y. Oct. 25, 2006).

IV. ARGUMENT

To state a claim under Section 10(b)[38] and Rule 10b-5,[39] a plaintiff must allege that the defendant "(1) made a misstatement or an omission of material fact (2) with scienter (3) in connection with the purchase or sale of a security (4) upon which the plaintiff reasonably relied and (5) the plaintiff's reliance was the proximate cause of their injury." *GSC Partners CDO Fund v. Wash.*, 368 F.3d 228, 236 (3d Cir. 2004). The failure to adequately plead any one of these essential elements necessarily precludes a securities fraud claim. *See In re Advanta Corp. Sec. Litig.*, 180 F.3d 525, 531 (3d Cir. 1999).

Here, the Amended Complaint is fatally deficient on three independent grounds. First, plaintiff has failed to plead an actionable misstatement or omission of material fact. Second, many of the statements challenged by plaintiff do not violate Rule 10b-5 because they are non-actionable statements of belief or opinion, forward-looking statements and/or statements of optimism. Third, plaintiffs have failed to plead particularized facts establishing a strong inference of scienter. For each of these separate and independent reasons, plaintiff's claims must be dismissed.

A. The Amended Complaint Fails To Plead A Misstatement Or Omission Of Material Fact

To plead a misstatement or omission of material fact, a plaintiff must allege with particularity facts showing that the statement is "factually inaccurate, or additional information is required to clarify it." *In re Discovery Labs Sec. Litig.*, No. 06-1820, U.S. Dist. LEXIS 79823, at

[38] Section 10(b) prohibits the "use or employ[ment], in connection with the purchase or sale of any security, . . . [of] any manipulative or deceptive device or contrivance in contravention of such rules and regulations as the [SEC] may prescribe . . . ." 15 U.S.C. § 78j(b).

[39] Under Rule 10b-5, it is unlawful to "make any untrue statement of a material fact or to omit to state a material fact necessary in order to make the statements made, in the light of the circumstances under which they were made, not misleading . . . in connection with the purchase or sale of any security." 17 C.F.R. § 240.10b-5.

* 27 (E.D. Pa. Nov. 1, 2006) (citation and internal quotation marks omitted). Where a plaintiff's allegations "arise from defendants' alleged failure to disclose facts necessary to clarify their otherwise . . . accurate statements of fact," the plaintiff "must, at a minimum, allege the existence of some fact, known to defendants at the time of the statements, whose disclosure would have made the statement clearer or more correct.." *Id.* In addition, the plaintiff must "demonstrate that, without this additional fact, a reasonable investor was likely to be misled by the statement." *Id.*

Here, plaintiff claims that, throughout the putative Class Period, defendants' public statements regarding the status of the Ampligen® NDA were false and misleading because they allegedly omitted the following facts:

(a) that the FDA advised Hemispherx of alleged deficiencies in its Ampligen® NDA;

(b) that the FDA asked Hemispherx for additional information; and

(c) that Hemispherx's need to remedy the alleged deficiencies would delay FDA's review of the application.[40]

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[40] Paragraphs 4 and 5 of the Amended Complaint encapsulate plaintiff's core allegations:

> 4. During the Class Period, Defendants misled investors regarding Hemispherx's New Drug Application ("NDA") for Ampligen which had been initially filed with the U.S. Food and Drug Administration ("FDA") as a treatment for CFS in 2007, on which FDA action was expected in February 2009.
>
> 5. Specifically, Defendants disclosed delays in FDA action on the Company's NDA saying explicitly that the delay would be brief and that the FDA did not request additional information at the time of the delays, while concealing deficiencies the FDA had noted previously, of which Defendants were well aware by virtue of the fact that they were then engaged in attempting to respond to them. During the Class Period, Defendants knew that the need to remedy these deficiencies would, at a minimum, delay FDA review and might result in rejection of the application if the FDA could not be satisfied.

(Exh. 1, Am. Compl. ¶¶ 4, 5.)

Yet, as detailed in Section II.B above, defendants, in fact, ***did*** disclose this information – promptly, fully and repeatedly – both before and during the Class Period. Soon after the FDA accepted the Ampligen® NDA for review on July 8, 2008, Hemispherx hosted an investor conference call during which Dr. Carter explained that the Company would be answering questions raised by the FDA that "were not critical for completeness but that remained important technical questions." (Exh. 72, 07/17/08 Conf. Call Tr. at 1.) He went on to explain that, although Hemispherx's goal was to submit new data in response to these questions within ten weeks, the Company had "up to six months" to provide the data. (*Id.*) Dr. Carter reported that these data included, *inter alia*, "further data from animal tests." (*Id.*)

Four months later, in November 2008, Hemispherx reported in its third quarter 2008 Form 10-Q that it had engaged Lovelace Respiratory Research Institute in Albuquerque, New Mexico ("Lovelace") to perform animal toxicology studies in support of the Ampligen® NDA. The Company explained that "[t]hese studies were requested by the FDA and will be done in collaboration with the resources of the New Brunswick facility. ***We expect these studies to be complete in January 2009***." (Exh. 7, 3Q 2008 Form 10-Q at 20 (emphasis added); *see also* Exh. 23, 11/18/08 Press Release (announcing the Lovelace studies).)

On January 29, 2009 – ***over six months*** after the FDA accepted the Ampligen® NDA for review and ***less than one month*** before the February 25 PDUFA date – Dr. Carter was asked during an interview whether additional tests would be needed to support the NDA. Dr. Carter responded that there were additional tests being conducted including animal tests for pre-clinical toxicology and that he anticipated ***4-8 weeks*** to complete those tests. (Exh. 91, 01.29.07 Inter. Tr. at 9.) Thus, at least as of January 29, 2009 – eleven days ***before*** the beginning of the putative Class Period – the market was well aware that (a) the FDA had asked Hemispherx to

conduct animal toxicology testing; (b) the Company had engaged a company to conduct the tests; and (c) the February 25, 2009 PDUFA date would likely be extended as a result.

On February 18, 2009 – the first day of the putative Class Period – Hemispherx announced in a press release that the FDA had extended the PDUFA date by three months to May 25, 2009. (*See* Exh. 26, 02/18/09 Press Release.) Plaintiff contends that this press release was "materially false and misleading" because it did not disclose that Hemispherx had submitted additional data to the FDA and that the Agency needed an extension of the PDUFA date in order to review the new data. (Exh. 1, Am. Compl. ¶¶ 47-48.) In fact, in both the February 18 press release and during a February 22, 2009 interview a few days later, Hemispherx explained that the FDA had extended the date in response to the Company's submission of additional data. (Exh. 26, 02/18/09 Press Release; Exh. 92, 02/22/09 Inter. Tr. at 7-10.)

Plaintiff also claims that the following statements, made by Dr. Carter during a March 19, 2009 investor conference call, were false and misleading: "We believe that we have answered all the major questions have been put forward with the Agency;" and "we believe that the major questions which they have asked have in our opinion been retired." (Exh. 1, Am. Compl. ¶ 52.) According to plaintiff, these statements were misleading because they did not disclose that Hemispherx "was then responding to numerous FDA requests for additional information concerning the Ampligen NDA." (Exh. 1, Am. Compl. ¶ 53.) Yet, contrary to plaintiff's contentions, Dr. Carter ***did*** disclose during the call that the Company was "continuing to provide brief reports, especially on animal data, to the Agency as has been requested." (Exh. 92, 03/19/09 Conf. Call Tr. at 2.) Indeed, Dr. Carter went on to explain that Hemispherx was "trying to anticipate questions that might come up in the future so that [it] [could] be prepared should there be further questions." (*Id.* at 12.) When asked what he thought was the likelihood

of FDA approving the Ampligen® NDA, Dr. Carter reiterated that "all we can do is cite historically data because obviously no one can read the future." (*Id.* at 14.)

In addition, plaintiff baldly alleges that the Company's explanation for the FDA's possible need for a 1-2 week extension of the May 25, 2009 PDUFA date – that "[r]eason for the possible delay was attributed by the Agency to certain staff scheduling changes" – was materially false and misleading. (Exh. 1, Am. Compl. ¶ 65.) Yet plaintiff cites to ***no*** facts, much less any that are particularized, showing that the FDA did ***not*** give this reason for needing more time.

Equally inadequate are plaintiff's accusations that Dr. Carter was lying when he stated on June 12, July 22, September 19, and October 9 that he had not heard from the FDA and did not know why. (Exh. 1, Am. Compl. ¶¶ 66-68, 70-72.) Plaintiff cites to no contemporaneous ***fact*** showing that Dr. Carter ***knew*** the reason for the delay.

Accordingly, plaintiff has failed to allege a material misstatement or omission, and the Amended Complaint should be dismissed.

B. Defendants' Statements Of Belief, Forward-Looking Statements And Statements Of Optimism Do Not Give Rise To A Securities Fraud Claim

1. Defendants' Statements Of Belief And Opinion Regarding Ampligens®'s Prospects For FDA Approval Are Not Actionable Under Rule 10b-5

Under the PSLRA's heightened pleading requirements, a plaintiff asserting a Rule 10b-5 claim based upon an alleged false statement of belief or opinion "'must allege with particularity provable facts to demonstrate that the statement of opinion is both objectively and subjectively false.'" *Podany v. Robertson Stephens, Inc.*, 318 F. Supp. 2d 146, 153-54 (S.D.N.Y. 2004) (quoting *Bond Opportunity Fund v. Unilab Corp.*, No. 99 Civ. 11074, 2003 U.S. Dist. LEXIS 7838, at *5 (S.D.N.Y. May 9, 2003) (citing *Virginia Bankshares, Inc. v. Sandberg*, 501

U.S. 1083, 1095-96 (1991))) (internal quotation marks omitted).[41] *See also, e.g., Ford Motor Co. Sec. Litig.*, 381 F.3d 563, 572 (6th Cir. 2004) (in 10b-5 action, statements of opinion are only actionable if speaker does not sincerely hold the opinion and the opinion is not factually well grounded); *see also In re Donald J. Trump Casino Sec. Litig.*, 7 F.3d 357, 372 n.14 (3rd Cir. 1993) (holding that although *Virginia Bankshares* concerned a claim under § 14(a) of Exchange Act, its reasoning is equally applicable to § 10(b) claims, but not reaching the question of whether the "subjective and objective falsity" pleading requirement applies to statements of opinion).[42]

In other words, a plaintiff must allege adequate facts showing ***both*** that the opinion had no basis in fact ("objective falsity") ***and*** that the speaker did not sincerely hold the opinion ("subjective falsity"). *See, e.g., In re Credit Suisse First Boston Corp. Analyst Reports Sec. Litig.*, 431 F.3d 36, 47 (2d Cir. 2005). If the complaint fails to plead either one of these elements, it must be dismissed. *See, e.g., id* at 53 (affirming dismissal of Rule 10b-5 claims based upon opinions where plaintiffs failed to plead sufficient facts showing subjective falsity); *Ford Motor*, 381 F. 3d at 572 (affirming dismissal of claims based on statements of opinion where plaintiffs failed to allege facts demonstrating that speaker did not believe statements made); *Podany*, 318 F. Supp. 2d at 153-54 (dismissing claims for failure to plead alleged fraudulent opinion with particularity).

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[41] In *Virginia Bankshares, Inc. v. Sandberg*, the Supreme Court held that, in actions brought under Section 14(a) of the Exchange Act, statements of opinion are only actionable if they are objectively and subjectively false. 501 U.S. 1083, 1095-96 (1991).

[42] *See also In re Credit Suisse First Boston Corp. Analyst Reports Sec. Litig.*, 431 F.3d 36, 47-48 (1st Cir. 2005) (citing *Virginia Bankshares, Inc. v. Sandberg*, 501 U.S. at 1095-96); *McGuire v. Dendreon Corp.*, 2009 U.S. Dist. LEXIS 124834 (W.D. Wash. May 21, 2009) (same); *In re JPMorgan Chase & Co. Sec. Litig.*, 2007 U.S. Dist. LEXIS 93877 (N.D. Ill. Dec. 18, 2007) (same); *Rubke v. Capitol Bancorp, Ltd.*, 551 F.3d 1156, 1162 (9th Cir. 2009) (same) (holding in § 11 securities action that statements of opinion are only actionable if objectively and subjectively false).

Here, plaintiff claims that defendants' expressions of belief or opinion regarding (1) whether any additional testing or documentation would be requested or required by the FDA prior to its Ampligen® NDA decision, (*see* Exh. 1, Am. Compl. ¶¶ 52, 68, 71, 90), and/or (2) when the FDA was expected to render that decision, (*see* Exh. 1, Am. Compl. ¶¶ 52, 68, 71), were allegedly false or misleading. Plaintiffs challenge, *inter alia*, the following statements of belief or opinion:

- "We [Hemispherx] ***believe*** that we have answered all the major questions that have been put forward with the agency [FDA]."
- "[W]e ***believe*** that the major questions which they [the FDA] asked have ***in our opinion*** been retired."
- "[W]e ***believe*** we're retiring them [any remaining FDA questions] through more comprehensive reporting."
- "[W]e ***believe*** the agency is substantially overworked at the moment. . . ."
- "[W]e ***believe*** that we've received the totality of significant questions and have retired them. . . ."
- "[W]e ***feel*** that if the – the appropriate course of action is is [sic] to be responsive to any queries, shall we say, that are still out there, and that's what we've been doing, as I said, providing definitive documents, where, before, there was [sic] summary documents, which we ***felt*** retired the issue. . . ."
- "We don't ***think*** that there are any documents [still requested by the FDA]. It's always hard to understand materiality. . . ."
- "The 438 [FDA inspection form] into the – into our facility, we retired, we ***believe, to the best of our satisfaction***, roughly a month or six weeks ago."
- "[I]f they [the FDA] deem – if they have a question, they ***may***- they ***may*** inspect again."
- "[O]bviously, Holister-Stier [the manufacturing facility that received the 438 form] has an excellent reputation in this field, and we ***think*** that, ultimately, that will carry the day."
- "[W]e continue to be in contact with the agency [FDA] concerning certain requests that they have made to us over the last year that have to do with

> what we call toxicology . . . and we ***expect*** sometime this quarter, the fourth quarter, to complete a set of requirements that have to do with . . . pre-clinical toxicology."

- "I'm very pleased to say that the clinical inspections resulted in no findings which required corrective action by the Company, which I ***believe*** is a very unusual positive result. . . ."
- "At the present time we are about to complete the remediation ***as we see it*** in the contract laboratory in Spokane [the Hollister-Stier lab]. I ***believe*** that in the next several weeks that work will be completed."
- "[W]e ***believe*** that we will have achieved everything ***to the best of our knowledge*** which is necessary for a completion of what we call pre-approval inspections by the agency. So we would ***expect*** at any time thereafter to receive final comments from the FDA."
- "I ***think*** that's an accurate summary," stated in response to an interviewer's question that purported to summarize the FDA's checklist for approving Ampligen®.

(Exh.1, Am. Compl. ¶¶ 52, 68, and 71 (emphasis added); *see* Exh. 73, 03/19/09 Conf. Call Tr. at 12; Exh. 74, 07/22/09 Conf. Call Tr. at 5, 7, 9, 10; Exh. 96, 10/09/09 Inter. Tr. at 8, 8-9, 10, 11, 12.)[43]

According to plaintiff, these statements of belief or opinion were materially false and misleading when made because defendants allegedly:

> misrepresented and concealed the fact that the Company need [sic] to submit multiple reports which were required by the FDA before the agency would act on the NDA, certain of which would take many additional months to produce, thus resulting in delay of FDA action by several months at a minimum.

(Exh. 1, Am. Compl. ¶ 72.)

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[43] Plaintiff also alleges in purported support of its scienter theory that Dr. Carter made the following statement during an April 9, 2008 investor conference call – one year prior to the putative Class Period: "[W]e do not ***believe*** any additional studies will be needed to complete the NDA filing status presumptively to go forward with a total application and receive a favorable review." (Exh. 1, Am. Compl. ¶ 90 (emphasis added); Exh.71, 04/09/08 Conf. Call Tr. at 4.) As explained in Section V.E, *infra*, this statement addresses the question of whether additional studies will be needed in order for the FDA ***to accept the NDA for filing***, and ***not*** as plaintiff insinuates, whether the Agency will require more studies for purposes of ultimate approval. Moreover, plaintiff has averred no facts showing that this statement was objectively and subjectively false when made. *See infra* Section IV.B.1.

Plaintiff's assertion completely mischaracterizes the facts as set forth in both the Amended Complaint and the documents incorporated therein. Defendants never guaranteed that ***no*** additional reports or information needed to be submitted to the FDA. As Dr. Carter consistently emphasized when discussing the status of the Ampligen® NDA during investor conference calls and interviews, he was only stating his ***belief*** that no ***major*** questions remained outstanding with the FDA.[44] Indeed, Dr. Carter repeatedly cautioned that the FDA might ask for more information from Hemispherx.[45] Moreover, as explained in Section IV.A above, plaintiff's allegation that Dr. Carter "concealed the fact that the Company need [sic] to submit multiple reports which were required by the FDA" is flatly contradicted by the undisputed fact of public record – and plaintiff's own allegations – that Dr. Carter ***repeatedly*** and ***publicly*** stated that Hemispherx ***was continuing to submit*** reports to the FDA:

- "[W]e feel that if the – the appropriate course of action is is [sic] to be responsive to any queries, shall we say, that are still out there, and ***that's what we've been doing***, as I said, ***providing definitive documents***, where, before, there was [sic] summary documents, which we felt retired the issue;"[46]

- "I don't -I don't want to suggest - and if I suggested it, that we are not in - we are not in correspondence with the agency, that would be [in]correct. ***We are regularly providing reports to the agency*** to different reviewers and different areas;"[47]

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[44] *See, e.g.,* Exh. 1, Am. Compl. ¶¶ 52, 68 ("We ***believe*** that we have answered all the ***major*** questions that have been put forward with the Agency;" "we ***believe*** that the ***major*** questions which they have asked have ***in our opinion*** been retired;" "we ***believe*** that we've received the totality of ***significant*** questions and have retired them. . . .") (emphasis added).

[45] *See, e.g.*, Exh. 1, Am. Compl. ¶¶ 68 ("We don't ***think*** that there are any documents [still requested by the FDA]. ***It's always hard to understand materiality***," "if they [the FDA] deem – if they have a question, they ***may*** – they ***may*** inspect again.") (emphasis added).

[46] Exh.1, Am. Compl. ¶ 68 (emphasis added); *see* Exh. 74, 07/22/09 Conf. Call. Tr. at 9.)

[47] Exh.1, Am. Compl. ¶ 68 (emphasis added); *see* Exh. 74, 07/22/09 Conf. Call Tr. at 9).

- "***[W]e continue to be in contact with the agency concerning certain requests that they have made to us over the last year*** . . . ."[48]

- "We ***continue to work with Hollister-Stier to finalize specific action***s to address the FDA Form 483 issues and Hollister-Stier ***has submitted a specific action plan*** to the Seattle, Washington office of the FDA."[49]

See also supra Sections II & V.A (listing numerous prior disclosures of reports being submitted by Hemispherx to FDA).

No reasonable investor would interpret Dr. Carter's repeated, consistent, and cautious expressions of opinion or belief on the status of the FDA's Ampligen® review in the manner that plaintiff alleges. Moreover, the Amended Complaint avers ***no*** particularized facts showing that these statements were objectively and subjectively false when made. Because plaintiff has failed to plead ***either*** element with respect to these statements, its claims must be dismissed.

2. Defendants' Forward-Looking Statements Regarding Ampligens®'s Prospects For FDA Approval Qualify For Protection Under The PSLRA's Safe Harbor And, Therefore, Are Not Actionable

(a) The PSLRA Requires That Courts Dismiss Claims Based On Forward-Looking Statements That Meet The Safe Harbor Criteria

To encourage public companies to disclose their own assessment of their future potential without fear of liability should their predictions turn out to be inaccurate, Congress included in the PSLRA a "safe harbor" for forward-looking information. *See Payne v. DeLuca,* 433 F. Supp. 2d 547, 560 (W.D. Pa. 2006) (quoting H.R., No. 104-369, at 43 (1995) (Conf. Rep.), *reprinted in* 1995 U.S.C.C.A.N. 730, 742); *see also Harris v. Ivax Corp.*, 182 F.3d 799,

[48] Exh.1, Am. Compl. ¶ 71 (emphasis added); *see* Exh. 96, 10/09/09 Inter. Tr. at 9.)

[49] Exh.1, Am. Compl. ¶ 69 (emphasis added); *see* Ex. 10, 2Q 2009 Form 10-Q at 22.)

806 (11th Cir. 1999) ("Congress enacted the safe-harbor provision in order to loosen the 'muzzling effect' of potential liability for forward-looking statements, which often kept investors in the dark about what management foresaw for the company.") This safe harbor "immunizes from liability any forward-looking statement, provided that: the statement is identified as such and accompanied by meaningful cautionary language; or is immaterial; or the plaintiff fails to show the statement was made with actual knowledge of its falsehood." *Institutional Investors Group v. Avaya, Inc.*, 564 F.3d 242, 254 (3d Cir. 2009).[50] Thus, statements meeting any of these criteria, as a matter of law, cannot support a Rule 10b-5 claim, and the complaint, to the extent it is based on any such statements must be dismissed. *See* 15 U.S.C.A. § 78u-5(e) ("On any motion to dismiss based upon subsection (c)(1), the court shall consider any statement cited in the complaint and any cautionary statement accompanying the forward-looking statement, which are not subject to material dispute, cited by the defendant.").

In accordance with the PSLRA's mandate, the Third Circuit has consistently upheld the dismissal of Rule 10b-5 claims that are based on forward-looking statements protected by the safe harbor. *See Avaya*, 564 F.3d at 257-58; *In re Discovery Labs. Sec. Litig.*,

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[50] Under the safe harbor, a reporting company and its officers, directors and employees may not, as a matter of law, be held liable for any prediction or other forward-looking statement which later prove to be inaccurate ***if***:

> (1) The forward-looking statement is "identified as a forward-looking statement, and is accompanied by meaningful cautionary statements identifying important factors that could cause actual results to differ materially from those in the forward-looking statement" (15 U.S.C. § 78u-5(c)(1)(A)(i)); ***or***
>
> (2) The forward-looking statement is "immaterial" (15 U.S.C. § 78u-5(c)(1)(A)(ii)); ***or***
>
> (3) The plaintiff fails to prove the forward-looking statement was made, or approved by an executive officer of the company, with actual knowledge that the statement was false or misleading. (15 U.S.C. § 78u-5(c)(1)(B)).

See Avaya, 564 F.3d at 254 n.18.

276 Fed. Appx. 154, 155 (3d Cir. 2008); *Key Equity Investors, Inc. v. Sel-Leb Mktg. Inc.*, 246 Fed. Appx. 780, 785-86 (3d Cir. 2007); *In re Merck & Co. Sec. Litig.*, 432 F.3d 261, 273 n.11 (3d Cir. 2005); *GSC Partners CDO Fund v. Washington*, 368 F.3d 228, 242-43 (3d Cir. 2004); *In re Advanta Corp. Sec. Litig.*, 180 F.3d 525, 536 (3d Cir. 1999). Thus, following Third Circuit precedent, courts in this District routinely dismiss claims based on forward-looking statements. *See, e.g., In re Nutrisystem, Inc. Sec. Litig.*, 653 F. Supp. 2d 563, 579-80 (E.D. Pa. 2009); *In re Aetna, Inc. Sec. Litig.*, No. 07-4451, 2009 U.S. Dist. LEXIS 48910, at *61-77 (E.D. Pa. June 9, 2009).

(b) Because Defendants' Forward-Looking Statements Qualify For Safe Harbor Immunity As A Matter Of Law, Plaintiff's Claims Must Be Dismissed

(i) Plaintiff's Claims Are Based, In Part, On Forward-Looking Statements

The PSLRA's safe harbor defines the term "forward-looking statement" to include, *inter alia*, the following categories of statements:

> (A) a statement containing a projection of revenues, income (including income loss), earnings (including earnings loss) per share, capital expenditures, dividends, capital structure, or other financial items;
>
> (B) a statement of ***the plans and objectives of management*** for future operations, including ***plans or objectives relating to the products*** or services of the issuer;
>
> (C) a statement of future economic performance, including any such statement contained in a discussion and analysis of financial condition by the management or in the results of operations included pursuant to the rules and regulations of the Commission;
>
> (D) any statement of the ***assumptions*** underlying or relating to any statement described in subparagraph (A), (B) or (C).

15 U.S.C.A. § 78u-5(i)(1)(A), (B), (C), (D) (emphasis added).

Plaintiff claims that defendants' forecasts regarding the timeframe for the FDA's Ampligen® NDA decision were false and misleading because these predictions did not take into account certain testing and documents the FDA requested in its Complete Response Letter that, according to plaintiff, were known to defendants during the putative Class Period. These forecasts include, *inter alia*, the following statements:

- "Yes, May 25, we would ***expect*** definitive response letters at that point."[51]
- "[W]e ***expect*** that sometime in the fall, perhaps sooner, we will be hearing from the – from the agency."[52]
- "It is our ***expectation*** that these issues will be resolved and we will be able to complete the resultant sequential validations by the end of 2009."[53]

All such statements are predictions of "the plans and objectives of [Hemispherx] management for future operations, including plans or objectives relating to ***the products*** [*i.e.*, Ampligen®] or services of [Hemispherx]," however, and therefore are deemed forward-looking under the PSLRA. 15 U.S.C.A. § 78u-5(i)(1)(B). Defendants' discussions of the assumptions underlying and relating to these statements, such as defendants' belief that no additional FDA testing or documentation would be required, are considered forward-looking as well. 15 U.S.C.A. § 78u-5(i)(1)(D).

(ii) Defendants' Forward-Looking Statements Were Identified As Such And Accompanied By Meaningful Cautionary Language

As explained above, forward-looking statements qualify for protection under the PSLRA's safe harbor so long as they are identified as forward-looking and "accompanied by

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[51] Exh. 1, Am. Compl. ¶ 52 (emphasis added); Exh. 73, 03/19/09 Conf. Call Tr. at 12.

[52] Exh. 1, Am. Compl. ¶ 68 (emphasis added); Exh 74, 07/22/09 Conf. Call Tr. at 5.

[53] Exh. 1, Am. Compl. ¶ 69 (emphasis added); Exh. 10, 2Q 2009 Form 10-Q at 22.

meaningful cautionary statements identifying important factors that could cause actual results to differ materially from those in the forward-looking statement." 15 U.S.C. § 78u-5(c)(1)(A)(i). Specifically, "[t]he cautionary language should be directly related to the alleged misrepresentations, but it does not have to actually accompany the alleged misrepresentation." *GSC Partners*, 368 F.3d at 243 n.3 (citations and internal quotation marks omitted). Therefore, a company's press releases and investor conference calls may incorporate by reference cautionary language contained in its SEC filings. *See, e.g.*, *Avaya*, 564 F.3d at 257 (finding that cautionary statements contained in corporate defendant's Form 10-Q, which were cross-referenced in defendant's conference calls and press releases, were sufficiently extensive and specific); *Merck*, 432 F.3d at 273 n.11 (finding that "[t]he cautionary language was sufficient because the press release incorporated by reference the cautionary statements in Merck's 2000 Form 10-K . . . ."); *Nutrisystem*, 653 F. Supp. 2d at 579 ("Cautionary language must be related to the forward-looking statements but need not actually accompany them.").

Moreover, while the cautionary language "must be extensive and specific," *Avaya,* 564 F.3d at 256 (quoting *GSC Partners CDO Fund v. Washington*, 368 F.3d 228, 243 n.3 (3d Cir. 2004)), a company need not warn against every possible risk or provide "a listing of all factors," *Ivax*, 182 F.3d at 807. As Congress explained, a "failure to include the particular factor that ultimately causes the forward-looking statement not to come true will not mean that the statement is not protected by the safe harbor." *Id.* (quoting H.R., No. 104-369, at 44 (1995) (Conf. Rep.), *reprinted in* 1995 U.S.C.C.A.N. 730, 743).

Here, all of defendants' predictions that plaintiff challenges (listed above) were identified as "forward-looking" and accompanied by meaningful cautionary language. At the beginning of the March 19, 2009 and July 22, 2009 investor conference calls, in which the first

two of the above statements were made, a spokesperson for Hemispherx explained that the call (or interview) would include forward-looking statements and identified "important factors that could cause actual results to differ materially from those in the forward-looking statement," 15 U.S.C. § 78u-5(c)(1)(A)(i):

> ***Information contained in this conference call other than historical information should be considered forward-looking*** and is ***subject to various risk factors and uncertainties***. For instance, the strategies and operations of Hemispherx involve the risk of competition, changing market conditions, change in laws and regulations affecting these industries, and ***numerous other factors discussed in this conference call, in the company's press releases, and the filings with the Security and Exchange Commission***. Just any specifically referenced investigational drugs and associated technologies of the company, including Ampligen, Alferon LDO, and Oragen are experimental in nature and as such are not designated safe and effective by a regulatory authority for general use and are legally available only through clinical trials with the referenced disorders.
>
> The forward-looking statements represent the company's judgment as of the date of this conference call. Any – the company disclaims, however, any intent or obligation to update these forward-looking statements. Clinical trials for other potential indications of the approved biologic Alferon N Injection do not imply that the product will ever be specifically approved commercially for other treatment indications. ***Similarly, the competition [completion] of the NDA filing process with Ampligen does not imply that the product will ever be approved commercially***.

(Exh. 74, 07/22/09 Conf. Call Tr. at 1 (emphasis added); *see also* Exh. 73, 03/19/09 Conf. Call Tr. at 1 (same).) In addition, forward-looking statements were identified and meaningful cautionary statements provided in the Company's second quarter 2009 Form 10-Q, which contained the third statement listed above. (*See* Exh. 10, 2Q 2009 Form 10-Q at 15-16 (identifying forward-looking statements), 29-41 (delineating risk factors).)

As permitted in the Third Circuit, the cautionary language provided in Hemispherx's conference calls and interviews also incorporated by reference the detailed list of

risk factors contained in the Company's 2008 Form 10-K, filed with the SEC on March 19, 2009. The "Risk Factors" section of the 2008 Form 10-K specifically warned investors that Hemispherx's forward-looking projections "involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of Hemispherx Biopharma, Inc. and its subsidiaries . . . to be materially different from any future results, performance or achievements expressed or implied" in that 10-K. (Exh. 8, 2008 Form 10-K at 1.)

The cautionary language contained in the Form 10-K was "extensive and specific" and "directly related" to the alleged defects in defendants' FDA approval projections. *GSC Partners*, 368 F.3d at 243 n.3. Plaintiff claims that defendants' forecasts regarding the timeframe for the FDA's Ampligen® NDA decision were false and misleading because these forecasts did not take into account certain testing and documents requested by the FDA prior to the Agency rendering any NDA decision. (*See* Exh. 1, Am. Compl. ¶¶ 48, 50, 53, 57, 60, 65, and 72.) Yet, Hemispherx's Form 10-K specifically warned investors that:

> ***Ampligen® may be found to be ineffective or to have adverse side effects, fail to receive necessary regulatory clearances, be difficult to manufacture on a commercial scale,*** be uneconomical to market or be precluded from commercialization by proprietary right of third parties. Our products are in various stages of clinical and pre-clinical development and, require ***further clinical studies*** and appropriate regulatory approval processes before any such products can be marketed. ***We do not know when, if ever, Ampligen® or our other products will be generally available for commercial sale for any indication. Generally, only a small percentage of potential therapeutic products are eventually approved by the FDA for commercial sale.***

(Exh. 8, 2008 Form 10-K at 14 (emphasis added).) Thus, Hemispherx's cautionary language is sufficiently meaningful under the PSLRA's safe harbor because it is "substantive, extensive and tailored to the future-looking statements they reference." *Avaya*, 564 F.3d at 258 (citation and

internal quotation marks omitted). Because Hemixpherx's cautionary language is sufficiently "meaningful" under the PSLRA, defendants' forward-looking statements are immune from liability under Rule 10b-5. Accordingly, plaintiff's Amended Complaint must be dismissed to the extent it relies on these forward-looking statements.

(iii) Defendants Are Immune From Liability Under The Safe Harbor For The Separate And Independent Reason That Plaintiff Has Failed To Show That Defendants Acted With Actual Knowledge

Even in the absence of meaningful cautionary language, a forward-looking statement is not actionable under Rule 10b-5 where, as here, the plaintiff's allegations fail to show that the defendant had "actual knowledge" that the statement, when made, was false or misleading. 15 U.S.C. § 78u-5(c)(1)(B); *see Avaya*, 564 F.3d at 274 (recognizing that liability for forward-looking statements "attaches only upon proof of knowing falsity"); *In re Discovery Labs. Sec. Litig.*, 2007 U.S. Dist. LEXIS 18163, at *6 (E.D. Pa. March 15, 2007) ("the burden is on plaintiffs to show that defendants ***knew*** the statement was false or misleading" (emphasis in original). Because plaintiff's conclusory assertions that defendants "knew" the alleged falsity of Hemispherx's forecasts regarding the Ampligen® NDA (*see* Exh. 1, Am. Compl. ¶¶ 48, 50, 53, 65, and 72) do not even support an inference of "recklessness," *see infra* Section IV.C, they fail to meet the safe harbor's higher "actual knowledge" standard. *See Avaya*, 564 F.3d at 259 n.29, 274. Thus, defendants are immune from liability for their forward-looking statements on this separate and independent ground.

(c) Defendants Had No Duty To Update Their Forward-Looking Statements

Once a company or its officers have made a forward-looking statement, they have no duty to update it. 15 U.S.C.A. § 78u-5(d) ("Nothing in this section shall impose upon any

person a duty to update a forward-looking statement."). Adhering to this statutory requirement, the Third Circuit has consistently held that that a company is not required to update forward-looking statements. *In re Burlington Coat Factory Sec. Litig.*, 114 F.3d 1410, 1433 (3d Cir. 1997) ("the voluntary disclosure of an ordinary earnings forecast does not trigger any duty to update"); *accord Advanta*, 180 F.3d at 536 (holding that the company had no duty to update a previously made forward-looking statement because it subsequently changed its business strategy); *In re CIGNA Corp. Sec. Litig.*, No. 02-8088, 2005 U.S. Dist. LEXIS 35524, at *13 (E.D. Pa. Dec. 23, 2005) (holding that "the law does not impose a duty to update forward-looking statements . . . with all relevant material information . . . .").

Equally well settled is the principle that companies are not obligated to update the public as to the state of the quarter in progress. *Burlington*, 114 F.3d at 1432; *see also Blum v. Semiconductor Packaging Materials Co. Inc.*, No. 97-7078, 1998 U.S. Dist. LEXIS 6868, at *7-9 (E.D. Pa. May 5, 1998) (holding that the failure to update the public in a mid-quarter press release that fourth quarter earnings would be below expectations, while the fourth quarter remained in progress, cannot give rise to a cause of action for securities fraud).

Thus, even assuming, hypothetically, that Hemispherx knew conclusively that the FDA would demand additional Ampligen® testing or documentation, or that the NDA would be delayed beyond a given PDUFA date, the Company had no duty to update its prior guidance. Indeed, Hemispherx's Form 10-K advised investors that:

> We do not undertake and specifically decline any obligation to publicly release the results of any revisions which may be made to any forward-looking statement to reflect events or circumstances after the date of such statements or to reflect the occurrence of anticipated or unanticipated events.
>
> . . . .

> [W]e undertake no obligation to update any forward-looking statement or statements to reflect events or circumstances after the date on which such statement is made or reflect the occurrence of unanticipated events.

(Exh. 8, 2008 Form 10-K at 1, 26.)

3. Several Of Defendants' Statements Of Belief And Forward-Looking Statements That Plaintiff Claims Violate Rule 10b-5 Also Constitute Immaterial Puffery And Are Non-Actionable For This Separate And Independent Reason

In the Third Circuit, "vague and general statements of optimism constitute no more than puffery and are understood by reasonable investors as such." *In re Advanta Corp. Sec. Litig.*, 180 F.3d 525, 538 (3d Cir. 1999). Therefore, "[s]uch statements *even if arguably misleading*, do not give rise to a federal securities claim because they are not material: there is no substantial likelihood that the disclosure of the omitted fact would have been viewed by the reasonable investor as having significantly altered the total mix of information made available." *Id.* (upholding dismissal of statements touting quality of company's credit and expertise of company's management as non-actionable puffery) (emphasis added) (internal quotation marks and citations omitted). Accordingly, district courts in this Circuit have consistently dismissed claims predicated on vague and general statements of optimism.[54]

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[54] *See, e.g., In re Loewen Group Inc. Sec. Litig.*, No. 98-6740, 2003 U.S. Dist. LEXIS 15680, at *49 (E.D. Pa. July 16, 2003) ("[S]tatement[] that. . . company is. . . 'pursuing transactions on a selective and disciplined basis' [is] nothing more that [sic] corporate puffery. These are the kinds of positive statements that corporate officers make all of the time and that reasonable investors know to take with a grain of salt."); *In re Viropharma, Inc. Sec. Litig.*, No. 02-1627, 2003 U.S. Dist. LEXIS 5623, *21 (E.D. Pa. April 7, 2003) ("everybody is a potential patient," drug is "a scientific revolution," and a "very exciting product" "must be dismissed as mere puffing."); *In re U.S. Interactive, Inc. Sec. Litig.*, No. 01-CV-522, 2002 U.S. Dist. LEXIS 16009, at *21, 34 (E.D. Pa. Aug. 23, 2002) (statement that company was "only Internet professional services firm" with "marketing skills, expertise in wireless and broadband technologies" was non-actionable puffery.); *accord In re Syntex Corp. Sec. Litig.*, 95 F.3d 922, 933-34 (9th Cir. 1996) (dismissing statements regarding potential success of generic drug as "optimistic speculations"); *In re Milestone Scientific Sec. Litig.*, 103 F. Supp. 2d 425, 458, 462 (D.N.J. 2002) (phrases "very excited," "very pleased," "tremendous excitement," "very positive," and "revolutionize" are non-actionable puffery); *In re Cybershop.com Sec. Litig.*, 189 F. Supp. 2d 214, 232 (D.N.J. 2002) (defendant made "optimistic, possibly even ambitious, statements that are necessarily immaterial as a matter of law. . . even if they reflect 'misguided optimism'"); *In re Eng'g Animation Sec. Litig.*, 110 F. Supp. 2d 1183, 1195 (S.D. Iowa 2000) (phrases "strong financial condition," and "business prospects remain excellent" do not give rise to a securities violation because

(continued...)

Courts are particularly wary of Rule 10b-5 claims that are based on optimistic statements regarding a drug's prospects for FDA approval. As Judge Posner has pointed out: "Everyone knows that the process of obtaining the FDA's approval for a new drug is fraught with uncertainty" *Lasalle v. Medco Research*, 54 F.3d 443, 445 (7th Cir. 1995). Therefore, to a reasonable investor, it should be "obvious" that pharmaceutical companies "[do] not control the pace of the FDA's consideration and therefore [can] not guarantee approval [of their new drug] by any date." *Id.* at 447. Moreover, investors expect corporate officers to express optimism about their company's business prospects. Indeed, "people in charge of an enterprise are not required to take a gloomy, fearful, or defeatist view of the future; subject to what current data indicates, they can be expected to be confident about their stewardship and the prospects of the business they manage." *In re AstraZeneca Securities Litig.*, 559 F. Supp. 2d 453, 471 (S.D.N.Y. 2008) (internal quotation marks and citation omitted).

Although it is obvious that a pharmaceutical company cannot guarantee how or when the FDA will decide a regulatory issue, plaintiff here has attempted to allege that the following optimistic statements regarding the future of Ampligen® and its potential for FDA approval violate Rule 10b-5:

- "Yes, May 25, we would expect definitive response letters at that point."[55]
- "[W]e expect that sometime in the fall, perhaps sooner, we will be hearing from the – from the agency."[56]

(continued...)

"[i]nvestors expect companies to think the best of themselves and predict growth"); *In re Cryomedical Scis., Inc. Sec. Litig.*, 884 F. Supp. 1001, 1020 (D. Md. 1995) ("hopeful statements" about medical device's "potential success" were non-actionable puffery).

[55] Exh. 1, Am. Compl. ¶ 52; Exh. 73, 03/19/09 Conf. Call Tr. at 12. *See infra* Section IV.B.2 (explaining that this statement is also forward-looking and protected under the PSLRA safe harbor).

- "[O]bviously, Holister-Stier [the manufacturing facility that received the 438 form] has an excellent reputation in this field, and we think that, ultimately, that will carry the day."[57]

- "I'm very pleased to say that the clinical inspections resulted in no findings which required corrective action by the Company, which I believe is a very unusual positive result. . . ."[58]

Because these statements are nothing more than general statements of optimism and puffery that no reasonable investor would consider material, they are deemed immaterial as a matter of law and cannot support a Rule 10b-5 claim. *See, e.g.*, *In re Syntex Corp. Sec. Litig.* 95 F.3d 922, 931, 933-34 (9th Cir. 1996) (dismissing claims based on "inactionable forecasts" and recognizing that a pharmaceutical company's optimistic statements about the potential success of its products must be viewed in context, including the fact that "drug companies are . . . subject to the influence of other unpredictable forces because their business is highly regulated"); *In re Bristol-Myers Squibb Sec. Litig.*, 312 F. Supp. 2d 549, 559 (S.D.N.Y. 2004) (holding that optimistic predictions of FDA approval were "non-actionable opinion, personal or corporate optimism and puffery"). For this separate and independent reason, plaintiff's claims based on these statements must be dismissed.

(continued...)

[56] Exh. 1, Am. Compl. ¶ 68; Exh. 74, 07/22/09 Conf. Call Tr. at 5. *See infra* Section IV.B.2 (explaining that this statement is also forward-looking and protected under the PSLRA safe harbor)

[57] Exh 1, Am. Compl. ¶ 68; Exh 74, 07/22/09 Conf. Call Tr. at 10. *See infra* Section IV.B.1 (explaining that this statement is also a non-actionable statement of belief.)

[58] Exh 1, Am. Compl. ¶ 71; Exh. 96, 10/09/09 Inter. Tr. at 8-9. *See infra* Section IV.B.1 (explaining that this statement is also a non-actionable statement of belief.)

C. The Amended Complaint Fails To Meet The PSLRA's Heightened Requirements For Pleading A Strong Inference Of Scienter

Under the PSLRA, a plaintiff must "state with particularity facts giving rise to a strong inference that the defendant acted with the required state of mind." 15 U.S.C. § 78u-4(b)(2). The Supreme Court has defined the required state of mind in Rule 10b-5 actions as the intention "'to deceive, manipulate, or defraud.'" *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, 551 U.S. 308, 313 (2007) (quoting *Ernst & Ernst v. Hochfelder*, 425 U.S. 185, 194 & n.12 (1976)). In the Third Circuit, "[t]his scienter standard requires plaintiffs to allege facts giving rise to a 'strong inference' of 'either reckless or conscious behavior.'" *Institutional Investors Group v. Avaya, Inc.*, 564 F.3d 242, 267 (3d Cir. 2009) (quoting *In re Advanta Corp. Sec. Litig.*, 180 F.3d 525, 534-35 (3d Cir. 1999)) (footnote omitted); *see also id.* at 274.[59] Reckless statements in this context do not involve

> "merely simple, or even inexcusable negligence, but an extreme departure from the standards of ordinary care, and which presents a danger of misleading buyers or sellers that is either known to the defendant or is so obvious that the actor must have been aware of it" . . . . "[C]laims essentially grounded on corporate mismanagement" do not adequately plead recklessness.

Id. at 267 n.42 (quoting *Avanta*, 180 F.3d at 535, 540).

To qualify as "strong" under the PSLRA, "an inference of scienter must be more than merely plausible or reasonable – it must be cogent and at least as compelling as any opposing inference of nonfraudulent intent." *Tellabs*, 551 U.S. at 314. This pleading requirement "obliges courts to weigh the 'plausible nonculpable explanations for the defendant's conduct' against the 'inferences favoring the plaintiff.'" *Avaya*, 564 F.3d at 267 (quoting

[59] The Supreme Court has not decided whether "recklessness" is sufficient to satisfy the scienter standard. *see Tellabs*, 551 U.S. at 319 n.3.

Tellabs, 551 U.S. at 324). A court considering the sufficiency of a plaintiff's scienter allegations "must engage in a comparative evaluation; it must consider, not only inferences urged by the plaintiff, . . . but also competing inferences rationally drawn from the facts alleged." *Tellabs,* 551 U.S. 308 at 314. Any "omissions and ambiguities" in a plaintiff's allegations "count against inferring scienter." *Id.* at 325. In short, the court must ask: "When the allegations are accepted as true and taken collectively, would a reasonable person deem the inference of scienter at least as strong as any opposing inference?" *Id.* at 326.

As explained below, plaintiff's scienter allegations (Exh. 1, Am. Compl.¶¶ 81-115) fail to satisfy the PSLRA's stringent standards for pleading the scienter element of its claim against defendants. For this reason alone, the Amended Complaint must be dismissed.

1. Plaintiff's Hindsight Allegations That Defendants *Knew* The FDA Would Request Additional Studies Before Approving Hemispherx's Ampligen® NDA Cannot Support A Strong Inference Of Scienter

In its Complete Response Letter, the FDA recommended that Hemispherx conduct (a) an additional (third) clinical trial of Ampligen® and (b) carcinogenicity studies on two rodent species. (Exh. 62, 12/01/09 Press Release.) Plaintiff baldly avers that defendants ***knew*** but did not disclose that the FDA would require these additional studies before it would approve Hemispherx's Ampligen® NDA. (Exh. 1, Am. Compl. ¶¶ 88-96.) Because the Amended Complaint contains no ***contemporaneous*** facts showing that defendants possessed any such knowledge during the putative Class Period, plaintiff's assertion is nothing more than impermissible "fraud by hindsight." *See, e.g.*, *Cal. Pub. Employees' Ret. Sys., v. Chubb Corp.*, 394 F.3d 126, 158 (3d Cir. 2004) ("We have been clear that fraud cannot be inferred merely because at one time the firm bathes itself in a favorable light but later the firm discloses that things are less than rosy. We have long rejected attempts to plead fraud by hindsight.") (internal

quotation marks and citation omitted); *GSC Partners CDO Fund v. Washington*, 368 F.3d 228, 239 (3d Cir. 2004) ("It is not enough for plaintiff[] to merely allege that defendants 'knew' their statements were fraudulent or that defendants 'must have known' their statements were false.")

Plaintiff's reliance on a statement of belief made by Dr. Carter's ten months ***before*** the beginning of the putative Class Period is completely misplaced. Plaintiff alleges that, during an April 9, 2008 investor conference call, Dr. Carter made the following statement: "[W]e do not ***believe*** any additional studies will be needed to ***complete the NDA filing status*** presumptively to go forward with a total application and receive a favorable review." (*See* Exh. 1, Am. Compl. ¶ 90 (emphasis added); Exh. 71, 04/09/08 Conf. Call Tr. at 4.) First and foremost, this statement plainly addresses the question of whether additional studies will be needed in order for the FDA ***to accept the NDA for filing***, and ***not*** whether the Agency will require more studies for purposes of ultimate approval. This is the only reasonable meaning since the Company had just submitted its NDA amendments and was awaiting word from the Agency as to whether it would accept the NDA for filing. Moreover, plaintiff has averred no particularized facts showing that this statement was either objectively or subjectively false when made (*see supra* Section IV.B.1 & n. 27.) Thus, this statement of belief cannot support an inference of scienter, despite plaintiff's conclusory allegations to the contrary. (Exh. 1, Am. Compl. ¶ 90.)[60]

Similarly inapposite is plaintiff's reliance on Dr. Carter's statements made during a December 3, 2009 investor conference, which occurred ***after*** the FDA issued its Complete Response Letter and ***after*** the end of the putative Class Period. During that call, Dr. Carter

[60] The averments of paragraph 90 are further misleading in that they allege that Dr. Carter made certain statement about Pfizer's Lyrica during the April 9, 2008 conference call when, in fact, he made no such statements during that call. (*See* Exh. 71, 04/09/08 Conf. Call. Tr.)

explained that the FDA had required another pharmaceutical company, Pfizer, to conduct an additional clinical trial when it was seeking approval of a fibromyalgia drug, Lyrica. (Exh.76, 12/03/09 Conf. Call Tr. at 3.) Plaintiff claims that Dr. Carter's comments show that he "knew of or recklessly disregarded that a third clinical trial, like the one required for Lyrica, would be needed for Ampligen, but Defendants filed the Ampligen NDA without performing this trial." (Exh. 1, Am. Compl. ¶ 89.) Yet, plaintiff has averred ***no*** particularized facts showing that Dr. Carter ***actually*** knew ***before*** receiving the Complete Response Letter that the FDA would ultimately require Hemispherx to conduct a third clinical trial prior to approval of the Ampligen® NDA. Indeed, the FDA determined that the NDA was sufficiently complete to permit a substantive review when it accepted the NDA for filing in July 2008, with two clinical trials supporting the application.[61] Thus, Dr. Carter's comments regarding the December 3 conference call do not support an inference of scienter.[62]

Finally, with respect to the carcinogenicity studies, plaintiff alleges that "Defendants knew that Hemispherx needed to perform carcinogenicity studies because the Company had requested a waiver from such studies, which was denied." (Exh. 1, Am. Compl.

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[61] In paragraph 95 and 96, plaintiff restates the fanciful theory that defendants filed the Ampligen® NDA with knowledge that the application would be rejected by the FDA. Plaintiff makes bald allegations that Hemispherx "would not have had the financial ability to conduct new clinical trials" absent the fund raising made possible by the NDA filing. Leaving aside the inherent unbelievably of such reasoning, plaintiff avers no particular facts in either paragraph indicative of what defendants knew or must have known with regard to the clinical trials, and, accordingly, neither paragraph contributes to the scienter analysis.

[62] Plaintiff also references the December 3 conference call in paragraphs 91 and 92 and broadly characterizes other statements, attributed to Dr. Carter, as stating that he "admitted that, at the time Hemispherx received the FDA's Complete Review Letter in December 2009, the Company had already engaged clinical review [sic] organizations ("CROs") to facilitate enrollment of patients for the third clinical trial prior to receiving the FDA's complete review letter." (Exh. 1, Am. Compl. ¶ 91.) There is no such statement in the transcript of the conference call. (Exh. 76, 12/03/09 Conf. Call Tr.) The only mention of CROs during the call was with regard to the company's plans for Alferon N, a product unrelated to Ampligen®. (*Id.* at 5.) Moreover, this statement was made by Dr. Strayer, rather than Dr. Carter. It would appear that the allegations in paragraphs 91 and 92 are erroneous, and they have no bearing whatsoever on the scienter analysis.

¶ 93.) In its December 1, 2009 press release, Hemispherx stated the following regarding the FDA's Complete Response Letter:

> In the Non-Clinical area, the FDA is recommending that the Company complete rodent carcinogenicity studies in two species. As part of the NDA submission, the Company had requested that these studies be waived, but the waiver has not been granted.

(Exh. 62, 12/01/09 Press Release.)

As explained in Section II, *supra*, Hemispherx requested a waiver of carcinogenicity studies when it filed its NDA in October 2007. (*See* Exh. 72, 07/17/08 Conf. Call Tr. at 6-7 (disclosing that the Company believed it had "compelling reasons" not to perform additional cancer studies but that its backup position was to request that these studies be done during the marketing approval stage); *see also* Exh. 70, 12/19/07 Conf. Call Tr. at 7-8 (discussing carcinogenicity issues); Exh. 71, 04/09/08 Conf. Call Tr. at 11 (same).) In its Complete Response Letter, the FDA advised Hemispherx that the Company's waiver request had been denied. (Exh. 62, 12/01/09 Press Release.) Because plaintiff has averred ***no*** facts showing that Hemispherx ***knew*** in advance of the Complete Response Letter that its waiver request would be denied, these allegations are nothing more than rank speculation and cannot support a strong inference of scienter.[63]

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[63] Nor should the speculative rantings by TheStreet.com's Adam Feuerstein, cited in the Amended Complaint (¶¶ 75, 80, 93), be included in the scienter analysis. (*See* Exh. 102, 11/03/09 TheStreet.com article; "Hemispherx Cops to Ampligen FDA Delay," *available at* http://www.thestreet.com/story/10620979/1/hemispherx-cops-to-ampligen-fda-delay.html (last visited Mar. 11, 2010); Exh. 103, 12/02/09 TheStreet.com article, "Hemispherx's Ampligen Dealt FDA Blow," *available at* http://www.thestreet.com/story/10636318/1/hemispherxs-ampligen-dealt-fda-blow.html (last visited Mar. 11, 2010).) Not only are Mr. Feuerstein's opinions bereft of any ***factual*** support, but they lack credibility as well. Indeed, another source upon which plaintiff relies, BioMedReports.Com, publicly questioned Mr. Feuerstein's integrity and competence as a columnist during the putative Class Period. (*See* 6/29/09 BioMedReports Article , Wall Street reporter's inaccurate reports are becoming patient safety issue claims biomedical company CEO," *available at* http://biomedreports.com/articles/most-popular/1683-reporters-inaccurate-articles-are-becoming-patient-safety-issue-claims-biomedical-company-ceo.html (quoting biomedical company CEO's statements that "[w]hen you haven't done your due diligence and you don't understand the basic chemistry of our product [and] you make recommendations [impugning the safety of a drug] (continued...)

2. Plaintiff's "Core Product" Allegations Do Not Support A Strong Inference Of Scienter

Plaintiff seeks to infer scienter merely from the fact that Ampligen® was one of Hemispherx's "core products" during the putative Class Period. (Exh. 1, Am. Compl. ¶¶ 97-103.) Yet district courts in this Circuit have consistently ***refused*** to impute to corporate officers any alleged "knowledge" that statements they made about their company's core business were allegedly false or misleading "absent particularized allegations showing that defendants had ***ample*** reason to know of the falsity of their statements." *In re Stonepath Group, Inc. Sec. Litig.* 2006 U.S. Dist. LEXIS 15808, at *36 (E.D. Pa. Apr. 3, 2006) (emphasis added); *accord City of Roseville Employees Ret. Sys. v. Horizon Lines, Inc.*, 2009 U.S. Dist. LEXIS 106186 at *52-*53 (D. Del. Nov. 13, 2009); *Grover v. DeLuca*, 2006 U.S. Dist. LEXIS 76093, at *32 (W.D. Pa. Sept. 9, 2006). Indeed, "[g]iven our Court of Appeals' recent reminder that "'generalized imputations of knowledge do not satisfy the scienter requirement regardless of the defendants' positions within the company,' caution is not simply prudent, it is required." *Stonepath,* 2006 U.S. Dist. LEXIS, at *36 (quoting *In re Alpharma Inc. Sec. Litig.*, 372 F.3d 137, 149 (3d Cir. 2004)).

Here, plaintiff has not – and as explained in Section IV.A *supra* – ***cannot*** allege any contemporaneous facts showing that the statements in question were false or misleading in the first instance. Without any factual allegations of falsity, there can be no "knowledge" of the alleged falsity to impute. Even assuming *arguendo* that defendants' statements were false or misleading, plaintiff has made no particularized allegations showing that defendants had ***any***

(continued...)

you are putting patient's safety at risk . . . There has to be a level of integrity in the research written and I think that's really lacking in their case.").)

reason, much less "ample reason," to know of the alleged falsity. For these reasons, plaintiff's core product theory of scienter must be rejected.

3. Plaintiff's Miscellaneous Knowledge Averments Fail To Support A Strong Inference Of Scienter

The "scienter section" of the Amended Complaint contains a variety of allegations that have little, if any, bearing on scienter. (*See* Exh. 1, Am. Compl. ¶¶ 86, 87, 97-103, 106-111, 112, 113-114.) First, plaintiff offers a statement by an alleged unnamed "witness" who claims to have "worked closely with Defendant Carter in an administrative capacity" – ***before*** the beginning of the putative Class Period. (*See* Exh. 1, Am. Compl. ¶ 86 (alleging that former employee worked at Hemispherx "from 1999 through the end of 2008").) The following averments constitute the sum total of this alleged witness's contribution to the Amended Complaint:

> That Dr. Carter tightly controlled the communication channel between Hemispherx and the FDA was an understatement. Everything went through him or not at all . . . . Dr. Carter did not want any of the information that was going back and forth to the FDA regarding Ampligen to get out into public knowledge until he wanted it to get out.

(*Id.*) This information "fail[s] to create the kind of detailed picture that is required to establish scienter under the PSLRA," *In re Adolor Corp. Sec. Litig.*, 616 F. Supp. 2d 551 (E.D. Pa. 2009), and therefore is meaningless. If anything, these allegations show that Dr. Carter was commendably careful about protecting Hemispherx's proprietary information.

Plaintiff next points to statements from Hemispherx's November 9, 2009 Form 10-Q regarding Key Man life insurance, which indicate that Dr. Carter was a key person in part because of "his being the co-inventor of Ampligen®, and his knowledge of [the company's] overall activities, including patents and clinical trials." (Exh. 1, Am. Compl. ¶ 87.) Because these allegations shed no light on Dr. Carter's knowledge of the FDA's review of the Ampligen®

NDA, they contribute nothing to the scienter analysis. Similarly, plaintiff alleges that "Defendant Strayer's scienter is supported by his role as Hemispherx's Medical director, in which he was responsible for and had control over the particular activities that [allegedly] were falsely reported to investors during the Class Period. . . ." (Exh. 1, Am. Compl. ¶ 103.) However, such "allegations that a securities-fraud defendant, because of his position in the company, 'must have known' a statement was false or misleading are . . . inadequate." *Advanta*, 180 F.3d at 539 (quoting *Maldonado v. Dominguez*, 137 F.3d 1, 10 (1st Cir. 1998)).

In addition, plaintiff attempts to support an inference of scienter by alleging that Dr. Carter and Dr. Strayer participated in "extensive" and "detailed" discussions regarding the Ampligen® NDA during frequent investor conference calls. (Exh. 1, Am. Compl. ¶¶ 97-103.) Rather than supporting a fraudulent motive, these allegations suggest that Drs. Carter and Strayer went out of their way keep the investing public informed.

Plaintiff also points to certain FDA publications and regulations and to Hemispherx's November 2, 2009 press release (Exh. 1, Am. Compl. ¶¶ 106-11) as purported support for its assertion that defendants waited until the November 2 press release to disclose, for the first time, "that Hemispherx had submitted numerous reports to the FDA during the Class period and was continuing to provide further reports on several topics" (Exh. 1, Am. Compl. ¶ 110.) Yet, as explained in Sections II & IV.A, *supra*, public record documents unequivocally show that Hemispherx promptly, fully and publicly disclosed – well before November 2 – the various reports listed in the November 2 press release. Because the Court need not accept as true any allegations that contradict these public documents, *e.g.*, *In re Yukos Oil Co. Sec. Litig.*, No. 04-CV-5243, 2006 U.S. Dist. LEXIS 78067, at *35 (S.D.N.Y. Oct. 25, 2006), plaintiff's assertions do not and cannot support an inference of scienter.

Plaintiff even attempts to plead scienter with the following statement allegedly made by Dr. Carter during a September 2009 investors conference when asked about the reasons for the delay in FDA action: "I don't know. I'm not sure. Perhaps it's because the Commissioner's husband worked for a hedge fund [which owned Hemispherx shares]." (Exh. 1, Am. Compl. ¶ 112.) Although plaintiff baldly alleges that this answer was "false," it points to no ***facts*** in support of this assertion. Instead, plaintiff merely rehashes its hindsight assertion that Dr. Carter "knew" the delay was the result of deficiencies ultimately identified in the FDA's Complete Response Letter. Mere speculation, however, will not support an inference of scienter.

Finally, plaintiff tries to plead a strong inference of scienter by citing warning letters Hemispherx received from the FDA in 1998 and 2000 regarding statements about Ampligen® that appeared on the Company's website – ***over ten years*** before the events giving rise to this action. (Exh. 1, Am. Compl. ¶¶ 113-114.)[64] Allegations of conduct outside the putative Class Period, however, do "***not*** satisfy the required pleading standard." *In re GeoPharma, Inc. Sec. Litig.*, 411 F. Supp. 2d 434, 450 (S.D.N.Y. 2006) (emphasis added). The old warning letters are particularly irrelevant to plaintiff's claims in that the FDA has not issued a warning to Hemispherx ***since*** 2000. Nor has the Agency ever stated or suggested that the Company's public statements about Ampligen® or the status of the Ampligen® NDA during the putative Class Period were either false or misleading. Indeed, ***had*** the FDA considered any such statement by Hemispherx to be false or misleading, the Agency would have contacted the SEC

[64] *See* Exh. 89, 1998 Warning Leter from Sherrie Shade, Regulatory Review Officer to William A. Carter (dated Oct. 15, 1998), *available at*, http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM168052.pdf; Exh. 90, 2000 Warrning Letter from Ele Ibarra-Pratt, Regulatory Review Officer to William A. Carter (dated July 2000), *available at*, http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM166046.pdf (last visited Mar. 11, 2010).

directly pursuant to inter-agency procedures established in 2004.[65] The fact that neither the FDA nor the SEC has determined that Hemispherx's statements about Ampligen® or the status of the Ampligen® NDA were false or misleading supports a strong inference of innocent – not fraudulent – conduct.

4. Plaintiff's Motive Allegations Undercut Rather Than Support Any Inference Of Scienter

Having failed to plead facts supporting a strong inference that defendants knew or must have known that the statements at issue were false or misleading, plaintiff attempts to fill this scienter void with allegations that the individual defendants were financially motivated to inflate the price of Hemispherx's stock. (*See* Exh. 1, Am. Compl. ¶¶ 82-85, 104-105.) Yet, motive allegations, alone, are no longer sufficient for pleading a strong inference of scienter. *Avaya*, 564 F.3d at 277 (citing *Tellabs*, 551 U.S. at 324). Indeed, even where (unlike here) a plaintiff does allege facts suggesting that a defendant had the requisite knowledge, additional allegations showing a plausible motive for fraud will not "bolster scienter" if the complaint, in its entirety, fails to support an inference that the defendant was "at least as likely as not to have acted on that motive and actually committed fraud." *Id.* at 278 (finding that the plaintiffs' motive allegations did not strengthen the inference of scienter).

Not only is motive insufficient by itself to plead a strong inference of scienter, but plaintiff's averments merely suggest that the individual defendants were motivated to increase the price of Hemispherx' stock and raise money for the Company. (*See* Exh. 1, Am. Compl.

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[65] In 2004, the SEC and the FDA developed a centralized procedure whereby the FDA refers to the SEC "possible instances of securities laws violations by public companies regulated by the FDA." (See Exh. 99, SEC/ FDA 02.05.04 Press Release, "SEC and FDA Take Steps to Enhance Inter-Agency Cooperation," available at http://www.sec.gov/news/press/2004-13.htm (last visited Mar. 11, 2010).) Thus, if the FDA determines that an applicant may be misrepresenting the status of its NDA or any aspect of its NDA or the proposed new drug, the FDA will share this information with the SEC and the SEC will investigate the matter.

¶¶ 83-85.) Such generalized motives are widely held by corporations and their executives and, therefore, have ***never*** supported an inference of scienter in this Circuit. *See, e.g., GSC Partners,* 368 F.3d at 237-38. Indeed, maintaining a high stock price "surely is the quintessential motive 'generally possessed by most corporate directors and officers.'" *In re Discovery Labs. Sec. Litig.*, 2006 U.S. Dist. LEXIS 79823, at *44 (E.D. Pa. Mar. 15, 2007) (citing *GSC Partners*, 368 F.3d at 237). Thus, because plaintiff's motive allegations fail to describe a concrete and personal benefit to the individual defendants, they necessarily "fail to contribute meaningfully to a 'strong inference' of scienter." *Avaya*, 564 F.3d at 279. *See also ECA & Local 134 IBEW Joint Pension Trust of Chi. v. JP Morgan Chase Co.*, 553 F.3d 187, 200 (2d Cir. 2009) ("Earning profits for the shareholders is the essence of the duty of loyalty, and therefore it would be an unusual case where accomplishment of this objective constitutes the requisite motive to defraud the shareholders.").

In fact, plaintiff's averments regarding Dr. Carter's Standby Financing Agreement ("Standby Agreement") with Hemispherx actually ***negate*** any inference of scienter. Plaintiff theorizes that, because Dr. Carter agreed to loan up to $1,000,000 in financing to the Company if it failed to otherwise achieve its financing goals, he had a motive to make false statements to assist the company in raising money through stock offerings. (Exh. 1, Am. Compl. ¶ 83.) What plaintiff fails to disclose in the Amended Complaint, however, are the important facts, set forth in Hemispherx's 2008 Form 10-K, that the Company (a) granted Dr. Carter 10-year warrants to purchase common stock in consideration for his entering into the Standby Agreement, and (b) also agreed to issue him secured notes with interest paid in common stock in the event a personal loan became necessary. (*See* Exh. 8, 2008 Form 10-K at 27, 42.) Accordingly, Dr. Carter's personal financial interest with regard to the Company's stock price remained aligned with that

of Hemispherx's shareholders regardless of whether he executed a personal loan. Had he attempted to jeopardize the Company's long-term success, as plaintiff baldly alleges, Dr. Carter would have harmed his own personal financial interest as well. Thus, plaintiff's theory that the Standby Agreement somehow gave Dr. Carter motive to commit fraud is completely irrational and unfounded and, therefore, weighs ***against*** any inference of scienter.

Similarly unavailing are plaintiff's allegations that the individual defendants were motivated to inflate the stock price merely in order to enhance returns from securities offerings during the Class Period. (Exh. 1, Am. Compl. ¶¶ 84-85.) "Corporate officers always have an incentive to improve the lot of their companies, but this is not, absent unusual circumstances, a motive to commit fraud." *Avaya*, 564 F.3d at 279. Plaintiff avers no facts suggesting that there were unusual circumstances with regard to defendants' efforts to raise capital, and its allegations of "a general corporate desire" on the part of defendants to "raise funds and obtain credit" cannot strengthen an inference of scienter. *Id.* at 278-79.

Equally inadequate are plaintiff's assertions that Drs. Carter and Strayer were motivated to advance the development and FDA approval of Ampligen® because they would receive bonuses if they achieved such corporate goals and objectives. (Exh. 1, Am. Compl. ¶¶ 104-05.) Like plaintiff's other motive averments, these allegations fail to suggest, much less strengthen, any inference of scienter because they merely reflect general motives common to most corporate officers. *E.g. Ind. Elec. Workers' Pension Trust Fund IBEW v. Shaw Group, Inc.*, 537 F.3d 527, 544 (5th Cir. 2008) ("Insofar as their executive compensation packages were tied to company performance, . . . [defendants] are in no different position than the vast majority of corporate executives. Consequently, this court has held that incentive compensation can hardly be the basis on which an allegation of fraud is predicated." (internal quotation marks

omitted)); *Wilson v. Bernstock*, 195 F. Supp. 2d 619, 636 (D.N.J. 2002) ("[C]ourts have uniformly held that incentive compensation alone cannot provide a sufficient basis on which to support allegations of a motive to create the illusion of corporate profitability, whether by active misrepresentation or wrongful nondisclosure of materially adverse information.").

In short, plaintiff's motive allegations support an inference of innocent rather than fraudulent conduct.

D. Plaintiff's Section 20(a) Claim Is Purely Derivative Of Plaintiff's Section 10(b) Claim And Must Be Dismissed

Plaintiff asserts a claim under Section 20(a) of the Exchange Act against Drs. Carter and Strayer. (Exh. 1, Am. Compl. ¶¶ 147-48.) To maintain its claim under Section 20(a), plaintiff must establish: (1) an underlying violation by a controlled person or entity; (2) that the defendants are controlling persons; and (3) culpable participation in the fraud by the controlling persons "'in some meaningful sense.'" *See, e.g., In re CDNow, Inc. Sec. Litig.*, 138 F. Supp. 2d 624, 644 (E.D. Pa. 2001).

Claims asserted under Section 20(a) are purely derivative. *Institutional Investors Group v. Avaya, Inc.*, 564 F.3d 242, 252 (3d Cir. 2009). Therefore, absent an underlying violation of the securities laws, there can be no controlling person liability. *Id.* at 280. Because plaintiff has failed to prove a claim under Section 10(b), its derivative claim under Section 20(a) against Dr. Carter and Dr. Strayer must also fail. *See In re Advanta Corp. Sec. Litig.*, 180 F.3d 525, 541 (3d Cir. 1999) ("claims under Section 20(a) are derivative, requiring proof of a separate underlying violation of the Exchange Act.").

V. CONCLUSION

For all of the above reasons, the Consolidated [Amended] Class Action Complaint should be dismissed with prejudice.

Respectfully submitted,

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Dated: March 12, 2010

CERTIFICATE OF SERVICE

I, William A. Liess, hereby certify that on March 12, 2010, I caused true and correct copies of Defendants' Motion to Dismiss Consolidated [Amended] Class Action Complaint, Memorandum of Law in Support, and Appendix to be served upon counsel for plaintiff as indicated below:

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